THE JOURNAL
of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 150, NO. 5 CHICAGO, ILLINOIS OCTOBER 4, 1952
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LYMPHOSARCOMA OF THE GASTROINTESTINAL TRACT

CHAIRMAN'S ADDRESS

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In the treatment of many malignant lesions certain criteria have been established that leave little or no doubt as to the proper procedure to be followed. This is not true in the treatment of lesions of the gastrointestinal tract, which cause a large percentage of all deaths from malignant lesions. From the therapeutic standpoint, the best attack on all malignant lesions of the gastrointestinal tract is that of surgical extirpation; however, in a certain number of radiosensitive tumors, namely the lymphoblastoma group, radiation therapy becomes an indispensable adjunct to surgery.

Lymphosarcoma is the commonest of the tumors arising from the lymphoid structure of the gastrointestinal tract and is the most frequent type of all sarcomas of the digestive system. Though all of the lymphoblastoma group may produce gastrointestinal disturbances by virtue of extrinsic pressure from enlarged retroperitoneal and mesenteric lymph nodes, lymphosarcoma frequently produces intrinsic deformity either as polypoid growths projecting into the lumen or as intramural lesions that infiltrate the wall. These lesions, in the beginning, may occur as a primary process in the bowel or as a part of a generalized lymphoid neoplastic disease. The two most recognized pathological types include the reticulum cell sarcoma (large round cell) and the malignant lymphocytoma (small round cell). Their presence in the lymphoid structures of the submucosa accounts for the early pain that is usually present owing to the involvement of the submucosal nerve plexuses. In addition to pain, which is frequently colicky in nature, there is usually an associated weight loss and mild secondary anemia. A palpable abdominal mass is frequently found, and the patient may have symptoms of a chronic progressive obstruction. Only in rare instances does an acute obstruction occur, and this is usually on the basis of an associated intussusception. Achlorhydria is common; melena is rare. Ulceration is uncommon but may occur owing to necrosis from pressure and loss of blood supply secondary to the lymphosarcomatous infiltration.

Roentgenologic studies of the stomach usually reveal characteristics of lymphosarcoma, but there are no pathognomonic findings. A diffuse infiltrating lesion often found in the distal portion of the stomach, particularly in the younger age group, would lead one to suspect this entity. The presence of exaggerated, stiffened rugae with diminished peristaltic activity and fixation are additional diagnostic features, but their absence does not rule out the possibility of this type of lesion. Polypoid growths are not distinguishable from carcinoma. The most frequent site of lymphosarcoma of the small bowel is the terminal ileum, where again the differential diagnosis both clinically and roentgenologically may be extremely difficult; the presence of pain is an important clinical feature in the differential diagnosis. There may be multiple sites of involvement, and, in contrast to carcinoma, there is usually an irregular dilatation of the involved segment rather than constriction; also the mucosal pattern is destroyed later, and the lesions are usually longer than those seen in carcinomatous infiltration of the bowel. Localized lymphosarcomatous masses of the intestine or mesentery may attain great size and frequently show rapid regression following radiation therapy. In the colon, though rare, these lesions most commonly occur in the cecum and usually present a polypoid appearance on the roentgenogram, which is often diagnosed as carcinoma until operation. Lesions of the rectum are usually accessible to proctoscopy, and diagnosis may be made by biopsy.

Surgical removal of the primary tumor, and involved lymph nodes wherever possible, together with postoperative irradiation comprises the most satisfactory form of treatment at the present time. The possibility of cure rests in the complete extirpation of the early lesions and immediate postoperative irradiation therapy. Exploratory laparotomy is justified not only in cases of suspected lymphosarcoma but also in those whose operability from a roentgenologic standpoint is questionable, since these lesions tend to remain confined to the involved portion of the intestine for a considerable length of time and metastasize relatively late as compared to that of carcinoma. Metastatic spread is through the lymphatics, making an intensive course of irradiation over the area of involvement as well as the anticipated area of spread advisable.

Read before the Section on Radiology at the 101st Annual Session of the American Medical Association, June 11, 1952.

Although there is still much controversy as to the relative radiosensitivity of the two histological types of lymphosarcoma, the consensus is that there is no remarkable difference in the prognosis of the two morphological types. Some feel, on the other hand, that prognosis depends more on the location of the lesions. Cecal lesions have the highest five year cure rate, whereas recurrence is more frequent in treated small bowel lesions, and lymphosarcoma of the rectum usually recurs in spite of adequate treatment. Owing to the relatively high degree of radiosensitivity of this type of new growth, frequently inoperable lesions and recurrent tumor masses will respond well to irradiation resulting in rapid reduction in size of the tumor, relief of the obstruction, and definite clinical improvement of the patient. Nitrogen mustards have been found to be of some avail in the treatment of recurrent lymphosarcoma that has become resistant to further roentgen therapy, and temporary remissions are frequently obtained; however, the results generally have been disappointing. Radioactive isotopes have not been significantly successful in combating this disease process to date. In a consecutive series of 100 cases of either lymphosarcoma, leiomyosarcoma, hemangioendothelioma, or fibrosarcoma of the gastrointestinal tract the following cases are of special interest.

REPORT OF CASES

CASE 1.—A white man, aged 58, when first seen on July 2, 1946, complained of weakness, a weight loss of 40 lb. (18.1 kg.), and upper abdominal pain for one year with no relationship to meals. Study of the gastrointestinal tract revealed a definite

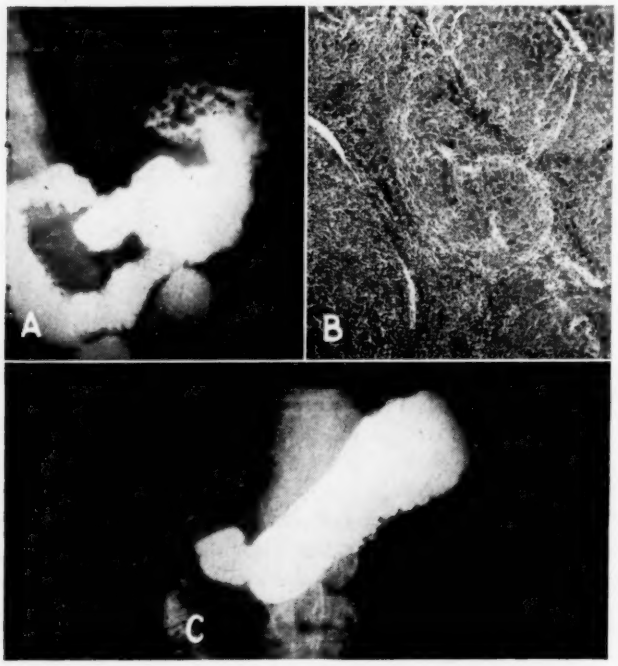

Fig. 1. (case 1).—*A*, invasive lesion of the greater curvature of the stomach, *B*, section of tumor showing lymphosarcoma, and *C*, following radiation therapy.

deformity in the contour of the stomach, most marked in the prepyloric area, with fixation and coarsening of the gastric rugae but no evidence of obstruction. The findings were indicative of a lymphosarcoma of the stomach. Surgical exploration revealed a large mass involving the walls of the stomach and lying in close association with the pancreas with numerous large lymph nodes scattered throughout the mesentery. Tissue was removed for biopsy, but no attempt was made at resection of the stomach because of the extensive involvement. Microscopic examination proved this to be a lymphosarcoma. Radiation therapy was begun the following day, and over a period of 90 days a total tumor dose of 4,000 r measured in air was given over upper abdominal ports. With transfusions and parenteral fluids the patient made a gradual recovery.

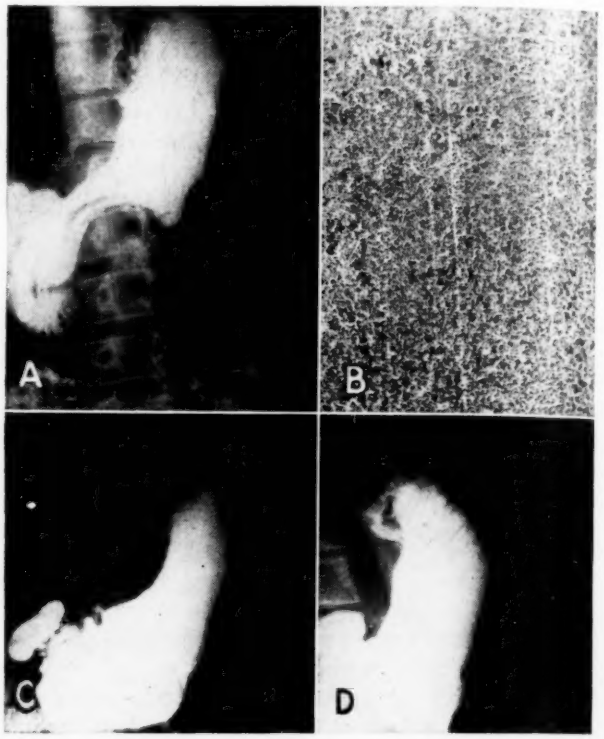

Fig. 2 (case 2).—*A*, primary lesion of the small intestine producing extrinsic pressure on the stomach, *B*, section of tumor showing lymphosarcoma, *C* and *D*, following radiation therapy.

He returned one year later with several large glands in both right and left cervical areas, each subclavicular region, and both axillas. These were treated with approximately 600 r measured in air to each area with complete regression of the nodes. Nine months later there was a recurrence of the adenopathy in the left cervical region. This was again treated with 600 r measured in air to each side of the neck with the same response as before. In June, 1950, approximately four years following the original examination, the patient returned for reexamination because of cough, and the chest roentgenogram revealed bilateral hilar and mediastinal adenopathy, for which further radiation was administered with suggestive improvement; however, death occurred a few months later. The periods between radiation therapy were relatively symptom free.

CASE 2.—A white woman, aged 47, on examination on Sept. 16, 1945, complained of indigestion, poor appetite, and weight loss, which had continued over a period of approximately eight months. There was a palpable abdominal mass. A study of the gastrointestinal tract revealed a definite deformity of the greater curvature of the stomach giving the impression that the stomach was riding over the mass in the abdomen. There was no pyloric or intestinal obstruction. The blood cell count revealed a moderate anemia. On surgical exploration, tissue was removed from a large mass involving the small bowel and mesentery, which proved to be lymphosarcoma; however, because of the extensive condition, the surgeon felt that the lesion was inoperable. At the time of surgery 28 radium needles containing 1 mg. of radium element to each centimeter of active length were inserted into the pedicle and tumor mass, and a total interstitial dose of 3,335 mg. was given. The patient improved markedly, and there was apparent regression of the tumor mass in the abdomen. Five months later there appeared to be an indefinite tumor mass in the abdomen, thought to be a recurrence of the

primary lesion, and at this time there was evidence of adenopathy in the left cervical area. Radiation therapy was again started, and the right and left cervical areas as well as the mass in the abdomen received approximately 600 r measured in air with good response.

The patient returned three months later complaining of a sore throat. On examination a large mass of tumor tissue in the left tonsillar fossa was found, and biopsy revealed this also to be a lymphosarcoma, which on treatment subsided. The patient remained reasonably well three years after the original diagnosis but later died of the disease.

CASE 3.—A white woman, aged 43, in December, 1944, complained of dull pain in the upper abdomen, weakness, tenderness, indigestion, and loss of weight and strength. On physical examination there was an apparent abdominal mass. X-ray examination revealed an extrinsic filling defect involving the mid portion of the transverse colon, and on surgical exploration a tumor mass was found involving the entire mesentery, which, on microscopic examination, proved to be a lymphoblastoma. Radiation therapy was started immediately, and approximately 8,000 r measured in air was delivered through eight abdominal ports with subsequent disappearance of the abdominal mass. The patient remained well until November, 1947, when she returned with a nodular mass in the left axilla. There was also involvement of both supraclavicular and inguinal areas. At this time approximately 1,000 r measured in air was delivered to each of the areas of involvement, and in 1949 she received further radiation to the right axillary mass. Again in 1950 she returned with bilateral cervical nodes and recurrence of the left axillary mass, which was treated with a good response. Within the past week the patient again returned with a rather large left sub-

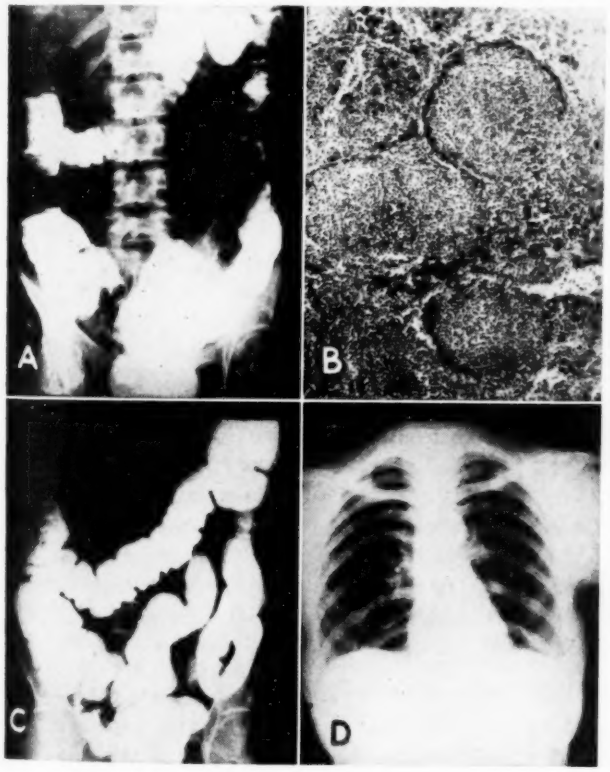

Fig. 3 (case 3).—*A*, primary lesion in the mesentery producing extrinsic filling defect in the mid portion of the transverse colon, *B*, section of tumor showing lymphosarcoma, *C*, filling defect no longer apparent after irradiation, and *D*, chest seven and one-half years after original diagnosis.

maxillary mass and small shotty right supraclavicular nodes and at the present time is having treatment over these areas. Her general condition is good seven and one-half years following diagnosis.

CASE 4.—A white woman, aged 48, was found to be healthy except for a firm resistant mass in the left upper quadrant extending down just below the umbilicus with several small tender areas. The hemoglobin level was 7.8 gm. (photoelectric colorimetric method with alkaline, 14.3 gm. per 100 cc. for women); red blood cell count, 3,300,000; and white blood cell count, 16,100. The differential, cell fragility, and platelet counts, and the prothrombin time were normal. The patient was given several blood transfusions, and, with the aid of the transfusions, the hemoglobin reached 11.8 gm., with 4,600,000 red blood cells

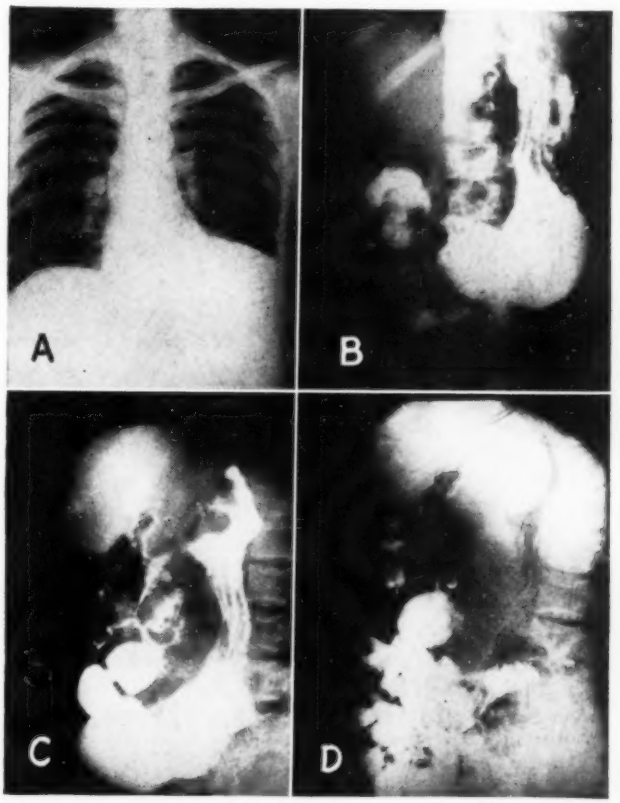

Fig. 4 (case 4).—*A*, elevation of the left side of the diaphragm because of massive lesion in cardiac end of stomach, and *B*, *C*, and *D*, massive invasion of the cardiac end of stomach by fibrosarcoma.

and 13,000 white blood cells. During her stay in the hospital she continued to run a low grade fever, and the clinical course was steadily downhill. The laboratory work showed a fairly marked dip in the hemoglobin level; shortly before death it was 30%. The pain in the upper left quadrant was the most prominent feature. She had essentially no gastrointestinal complaints nor had she any blood in the urine, and the mass in the left upper quadrant continued to grow in size. The patient died, and at autopsy it was found that the mass in the left upper quadrant actually was a tumor mass of the stomach. The lesion was adherent to the diaphragm and to the adjacent peritoneal structures. There were multiple metastatic nodules in the abdomen and in the liver, and the microscopic diagnosis shows a primary myofibrosarcoma in the fundus of the stomach.

Although the ultimate prognosis in patients with lymphosarcoma is grave, many of these persons, under close observation and with repeated courses of x-ray therapy, have many years of relatively comfortable and symptom-free life and carry on their normal activities. It is my opinion that the most satisfactory treatment to date for lymphosarcoma primarily involving the gastrointestinal tract and its adjacent structures is that of surgical extirpation of as much of the tumor and involved lymph nodes as possible, followed by an intensive course of irradiation therapy with nitrogen mustard held in reserve for radioresistant cases or for those whose lesions become resistant following repeated courses of roentgen therapy.

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HIDDEN OR UNSUSPECTED BRONCHIECTASIS IN THE ASTHMATIC PATIENT

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Chronic irritation causes muscle spasm, and prolonged muscle spasm augments chronic irritation. The bronchial musculature is not excepted from this interreactive phenomenon. The classical symptoms of bronchiectasis—cough, hemoptysis, and production of purulent sputum—are irritative factors that can, and frequently do, produce bronchospasm. Conversely, chronic or recurrent bronchospasm can produce bronchial obstruction and resultant infection. Whether it be the inaugurative or the secondary source of infection, bronchiectasis not only joins but also maintains this vicious disease cycle, although, unfortunately, its identity may be hidden behind the paroxysms of dyspnea and wheeze (often called bronchial asthma).

The asthmatic patients we have seen at the Overholt Thoracic Clinic are classified as medical failures, since they have not responded favorably to conservative therapy. Their previous medical treatment has included bronchodilatory and expectorant drugs, desensitization measures, changes in climate, psychotherapy, antibiotics, corticotropin (ACTH), and cortisone. In addition, several have had surgical measures for asthma, such as sinus drainage and the removal of teeth, hemorrhoids, prostatic tissue, gallbladder, and nasal polyps. This surgery had been performed not only in an attempt to clean up a specific infectious problem but also in the hope that it would remove a possible "trigger mechanism" that might have set off the asthmatic attacks. In this group of patients, these measures had failed to alter the attacks of bronchospasm. The symptoms of cough, hemoptysis, purulent sputum, wheeze, and dyspnea are primarily pulmonary in origin, which suggests that any source of asthmatic excitation would probably be located in the pulmonary system. A complete examination of the bronchopulmonary system is therefore indicated when searching for such a trigger mechanism or focus of infection.

Bronchial obstruction, partial or complete, is responsible for many of the clinical manifestations of bronchial asthma. A reduction in the lumen impairs ventilation and gaseous interchange, which, in turn, is followed by changes in the circulatory dynamics. The bronchus may be obstructed by spasm, fibrostenosis, a foreign body, or lymph nodes, which may compress, encircle, or perforate the bronchus. Often these factors combine to produce bronchiectasis. Bronchial segments are oftenest affected, and they may be completely or partially obstructed, with resultant atelectasis or emphysema. With structural changes in one or more segments, there is an increase in the negative intrapleural pressure, with a greater dilating effect on adjacent segments. The altered mechanics make it more difficult for the patient to raise secretions. Mucosal edema adds to the bronchial obstruction. The infection and inflammatory changes that result from retained secretions promote the formation of bronchiectatic segments or subsegments. The occurrence of these changes near the segmental or lobar orifice may produce a fibrostenosis and thus permit the development of bronchiectasis distal to the stenosis. Lymph nodes may become enlarged, fibrotic, or calcified because of repeated pulmonary infections or tuberculosis. The calcified nodes may erode into a bronchus and cause partial or complete obstruction, with retained secretions and bronchial infection.

Prickman and Moersch [1] studied 140 asthmatic patients bronchoscopically and observed a definite stenosis in 60 of them. We have not noted such a high incidence of stenosis in asthmatic patients at this clinic. Brock [2] and Graham [3] noted that the middle lobe bronchus is surrounded by nodes at its take-off from the stem bronchus, and it is these nodes that not only drain the middle and lower lobes but often drain the right upper lobe. In addition, the middle lobe bronchus is long and narrow and has thin walls, all of which make it susceptible to compression by enlarged hilar nodes. Mechanical obstruction has also been found in the lingula pulmonis and may actually occur in any part of the bronchial system together with combined asthma and bronchiectasis. A study of the clinical histories of asthmatic patients reveals that the primary symptom may be either bronchospastic or bronchiectatic in nature. The important point is that in an asthmatic person the presence of bronchiectasis is of grave concern, no matter how small the involvement. The constant irritation of the bronchial system with cough and purulent or bloody secretions constitutes an abnormal stimulus that eventually causes bronchospasm; and, as already noted, the coexistence of bronchospasm and bronchiectasis forms a vicious cycle, with each phase stimulating the other.

DIAGNOSTIC AND THERAPEUTIC PROCEDURES

Bronchiectasis is a segmental disease, and it may be present in any one of the 18 segments of the two lungs. In 35 to 50% of the cases, it occurs bilaterally. The most commonly affected segments are the basal groups, the lingula, and the middle lobe. The bronchial deformity may be cylindric, fusiform, or saccular; usually, the immediately surrounding parenchyma is normal. Hemoptysis, purulent sputum, repeated pulmonary infections, and localized physical findings over the lung fields strongly suggest the presence of bronchiectasis, especially in asthmatic patients. In many instances the clinical diag-

From the Department of Surgery, Tufts College Medical School, and the New England Deaconess and New England Center hospitals.

Read before the Section on Diseases of the Chest at the 101st Annual Session of the American Medical Association, Chicago, June 11, 1952.

1. Prickman, L. E., and Moersch, H. J.: Bronchostenosis Complicating Allergic and Infectious Asthma, Ann. Int. Med. **14**: 387 (Sept.) 1940.
2. Brock, R. C.: Post-Tuberculous Broncho-Stenosis and Bronchiectasis of the Middle Lobe, Thorax **5**: 5 (March) 1950.
3. Graham, E. A.; Burford, T. H., and Mayer, J. H.: Middle Lobe Syndrome, Postgrad. Med. **4**: 29 (July) 1948.

nosis of bronchiectasis in an asthmatic person is not easy to make, for the superimposition of anatomic abnormalities can be confusing not only acoustically but also visually. Roentgenograms, especially with contrast media, must be interpreted with the knowledge that bronchospasm can alter the abnormal image from that of uncomplicated bronchiectasis.

Bronchoscopy is performed for diagnostic and therapeutic reasons. It may reveal the source of purulent sputum or pulmonary bleeding and at times may impress the observer with the significance of the presence of minimal bronchiectasis. Bronchoscopy may show bronchostenosis, the presence of a foreign object, or the effect of lymph nodes either by compression or perforation. Attempts to dilate fibrostenosis is no longer our practice. Temporary benefit is often given through the removal of tenacious and viscid secretions by bronchoscopic aspirations, which may be repeated and sometimes are done under deep ether anesthesia. However, it is bronchography that is the key to accurate appraisal of the asthmatic patient for the presence or absence of bronchiectasis. It is often a difficult procedure and may need to be repeated before a satisfactory bronchial pattern is obtained. The patients are questioned as to drug sensitivities, since fatalities have been reported, supposedly from iodized oil (lipiodol®) or cocaine reaction. For the examination, local anesthesia, usually cocaine, is generally satisfactory; only with immature persons below teen age has general anesthesia been necessary.

Fig. 1.—Bronchogram showing that sufficient contrast medium has been injected to give complete pattern, but procedure is diagnostically worthless because of marked bronchospasm.

Preparation for bronchography requires hospitalization, bronchodilators, antibiotic drugs, and bronchoscopic aspiration. If bronchoscopy reveals marked spasm and tenacious secretions, the injection of contrast medium is postponed; and bronchography is never attempted on a patient who is having moderate or serious respiratory distress, since the injection of contrast medium may increase embarrassment of the ventilatory system. At times, with apparently adequate preparation, so much spasm may develop during the injection that only main-stem bronchi are outlined (fig. 1). Incomplete bronchograms are of poor diagnostic value, and a repeat

Fig. 2 (case 1).—Roentgenogram shows apparently normal chest, indicating need for further examination in determining presence of bronchiectasis. (See figure 3.)

Fig. 3 (case 1).—Bronchogram showing extensive bronchiectasis of basal segments and lingula.

examination should be done. Haphazard and inadequate preparation for bronchography is not only dangerous, but it seldom reveals the trigger mechanism, i. e., bronchiectasis, in the asthmatic patient. Di Rienzo [4] has stressed the importance of the dynamic and tonic phenomena of the bronchi that are revealed by bronchography: (1) the evident reduction of the caliber of the bronchial branch of the second, third, or fourth order in one segment or zone of the lung; (2) the absence of fine branching in the terminal portions of the affected lung segment; (3) the lack of foliage in this area; (4) the great delay in progression of the contrast media in the abnormal segments; (5) the presence of numerous bubbles; (6) the unchanged caliber of the inflated bronchus during inspiration and expiration; and (7) the almost complete loss of movement of the bronchial tree in the affected area due, in part, to spasmodic rigidity of the bronchus and inadequate excursion of the diaphragm.

The changes and findings observed on the fluoroscopic screen during the injection of the contrast medium should be recorded for correlation with x-ray, bronchoscopic, and clinical findings, so that the diseased segments may be identified and located. Once bronchiectasis has been demonstrated, the treatment is surgical unless the disease is too extensive or the general status of the patient is too poor to permit surgery. Experience in treating bronchiectasis by excision has repeatedly demonstrated that a good final result depends not only on the excision of disease tissue but also on the conservation of all normal tissue. Segmentectomy permits the thoracic surgeon to follow these two fundamental concepts. Below are case reports of four asthmatic patients who responded favorably to surgical treatment for bronchiectasis.

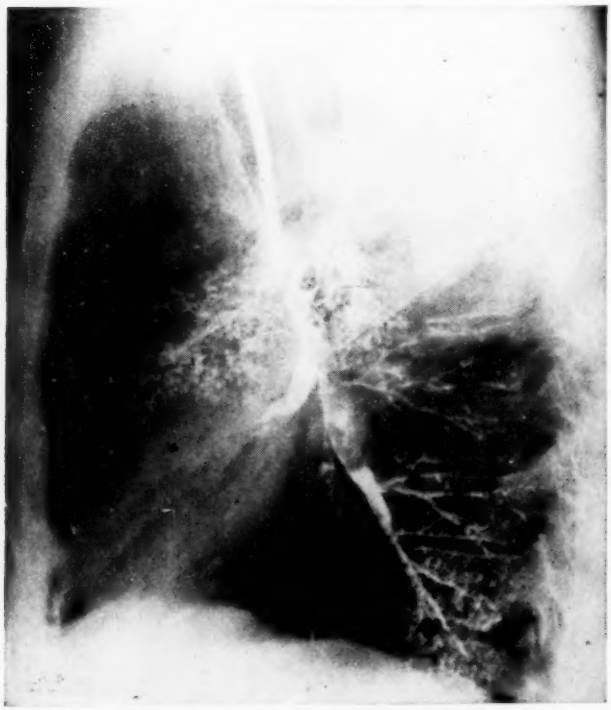

Fig. 4 (case 2).—Bronchogram demonstrating nonfilling of middle lobe and anterior basal segment of lower lobe by contrast medium.

4. Di Rienzo, S.: Radiologic Exploration of the Bronchus, Springfield, Ill., Charles C Thomas, Publisher, 1949, p. 190.

REPORT OF CASES

CASE 1.—A 23-year-old woman, single, had a severe respiratory infection at the age of 6 that required several months' bed rest for its treatment. Since that time she had had a chronic cough that was productive of several ounces of purulent sputum daily. At the age of 18 she had pneumonia, following which a marked wheezing developed that was usually severer on the left side. She had progressive dyspnea but no hemoptysis. Bronchodilating drugs, expectorants, and other measures that included an autogenous vaccine were employed over a three year period. There was no significant improvement. Antibiotics and postural drainage did diminish the severe wheezing and dyspnea, however, Chest roentgenogram (fig. 2) was normal, but bronchography revealed saccular bronchiectasis involving the basal segments of the left lower lobe and the lingula (fig. 3). In April, 1951, the involved segments were removed. Convalescence was uneventful. The patient has since been continuously free from wheeze and purulent sputum.

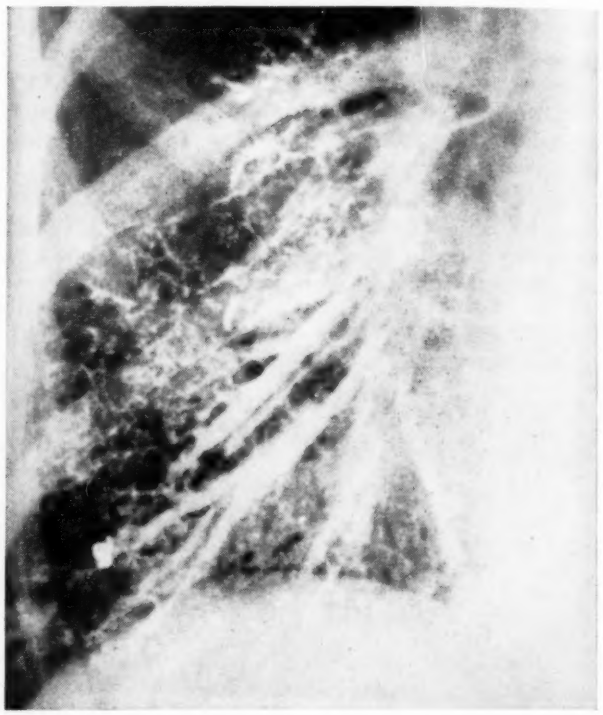

Fig. 5 (case 3).—Bronchogram revealing cylindric bronchiectasis in basal segments of right lower lobe. Patch of marked density in costovertebral angle is an artefact.

CASE 2.—A man, aged 59, worked as a janitor for 15 years without any pulmonary symptoms. Attacks of severe wheezing and dyspnea then gradually developed without any apparent cause, and for 18 months he was able to work for only a few weeks at a time. He lost 10 to 12 lb. (4.5 to 5.4 kg.) in weight in one year. At first, epinephrine (adrenalin®) and aminophylline were of benefit but soon became ineffective. An allergy checkup was of little help. Approximately six months after the first attacks of wheezing, the patient was treated for a virus infection; following this he had a chronic cough that was productive of 8 to 10 cc. of purulent sputum each morning. Chest roentgenogram was normal. Because of intense bronchospasm, bronchography had to be done three times, and abnormality of the middle lobe bronchus was finally demonstrated (fig. 4). Exploratory thoracotomy was done in December, 1948, and a contracted, airless, solid, and functionless middle lobe was found. A ring of enlarged lymph nodes was obviously obstructing the middle lobe bronchus by external pressure. There were no other abnormalities, and the middle lobe was removed without difficulty. The patient was discharged from the hospital on the 11th postoperative day and has been completely free from cough, purulent sputum, wheeze, and dyspnea since surgery. He is back to normal weight and has not lost time from work.

CASE 3.—A married woman, aged 46, was first seen in 1950 complaining of severe attacks of wheezing and dyspnea of two years' duration following the aspiration of a peanut that she believed was coughed up. Within a few weeks, attacks of wheezing developed and were soon followed by a "bronchitis and virus infection." Bronchoscopy was done several weeks later with completely negative findings. She was sensitive to silk and house dust, but desensitization measures were of no benefit. The wheeze and dyspnea became progressively worse and showed little or no response to treatment with bronchodilators. There was also no favorable response to change in diet, climate, and use of autogenous vaccine. At the end of one year, the patient began to have frequent respiratory infection and to raise a small amount of purulent sputum. The wheezing was bilateral and did not disappear with raising of sputum. A repeat bronchoscopy demonstrated purulent secretions in the right lower lobe bronchus, and bronchography revealed bronchiectasis of the basal segments of the right lower lobe (fig. 5). At thoracotomy of the right side in April, 1950, there was definite, palpable nodulation beneath the diaphragmatic surface of the basal segments of the lower lobe, while the remainder of the lung was normal. A basal group segmentectomy was done, and the patient was discharged from the hospital on the 12th postoperative day. She has had no asthmatic or other pulmonary symptoms since surgery.

CASE 4.—The patient, a man, was first seen in 1942 at the age of 32 complaining of severe wheezing and dyspnea of two years' duration. He responded fairly well to frequent injections of epinephrine and aminophylline. About two months before hospital admission he contracted a cold and soon afterwards began to cough and raise large quantities of purulent sputum. He was then hospitalized in status asthmaticus, and roentgenogram and bronchoscopy demonstrated a large abscess in the right upper lobe. This was drained, and within a few days the patient was relatively free of wheezing. The drainage tract was healed in a few months, and he was not seen again until November, 1949. At that time he complained again of progressively severe attacks of wheezing, dyspnea, and a cough that was productive of a small amount of purulent sputum. He was using epinephrine, aminophylline, and orally administered bronchodilators many times a day with only a few minutes' relief. A trip to Arizona and a change in diet had not changed the course of the patient's asthma. He had been unable to work for two years. At bronchoscopy, purulent secretions were seen at the right upper lobe orifice, and bronchography demonstrated a 4 cm. cavity in the right upper lobe connecting with the apical bronchus (fig. 6). Minimal cylindrical bronchiectasis was present in the posterior basal segment of the left lower lobe. At thoracotomy dense adhesions were encountered over the right upper lobe, the cavity was easily palpable in the upper lobe, and the upper and middle lobes would not expand on positive pressure. The right upper and middle lobes were removed. The patient's postoperative course was uneventful, and he was discharged from the hospital on the 14th postoperative day. Since then he has been employed as a clerk in a grocery store (fig. 7) and during the past two and one-half years has been absent from work a total of only two weeks because of colds. He occasionally uses aminophylline suppositories or "luasmin" (a sedative containing theophylline sodium acetate, ephedrine sulfate, and phenobarbital sodium).

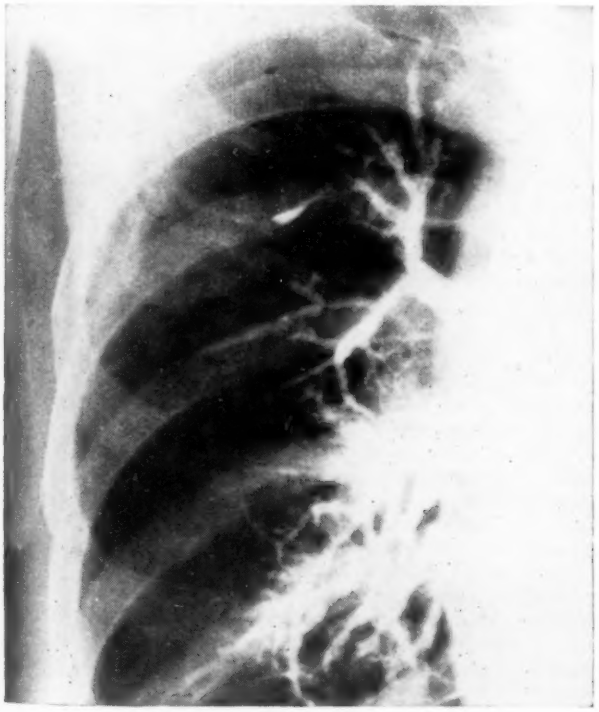

Fig. 6. (case 4).—Bronchogram demonstrating apical bronchus of right upper lobe connecting with a cavity, and abnormal pattern of middle lobe area.

Fig. 7 (case 4).—Photographs of patient following segmentectomy for bronchiectasis. Arrows indicate line of incision at thoracotomy (posterior) and abscess drainage (anterior).

THERAPEUTIC RESULTS

During the period from Jan. 1, 1948, to Jan. 1, 1952, 76 patients with severe bronchial asthma were treated at this clinic. Bronchiectasis had been suspected in only four of these patients prior to our seeing them. One patient had an adequate bronchogram that demonstrated bilateral bronchiectasis. The other bronchograms were unsatisfactory. Bronchography was done on 75 patients without ill effects and revealed bronchiectasis in 27, of whom 13 had the disease bilaterally. Exploratory thoracotomy was done on the 27 bronchiectatic patients, all but one of whom were treated by excision of the diseased tissue. (In this one patient the disease was too extensive for removal.) Four of the 13 patients with bilateral bronchiectasis were treated by bilateral resection. Two patients suffered infectious complications postoperatively and were not improved. Twenty of the 26 patients treated surgically are greatly improved in health and are able to work; only 7 require bronchodilator drugs.

SUMMARY

Bronchiectasis, hidden and unsuspected, is often present in the asthmatic patient. Removal of the abnormal segments can bring permanent relief.

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PYLORIC STENOSIS SECONDARY TO HYDROCHLORIC ACID INGESTION

REPORT OF TWO CASES IN WHICH HEPATITIS DEVELOPED

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Ingestion of concentrated mineral (hydrochloric and sulfuric) acid frequently results in severe damage to the stomach but only minor and infrequent damage to the esophagus. This is surprising since the general conception is that corrosive ingestion leads predominantly to esophageal injury and stenosis. This is true of concentrated alkalis but apparently not for concentrated acids. This report of two cases with almost complete pyloric obstruction without permanent esophageal injury is prompted by the paucity of such reports in the English literature, by the excellent results following gastroenterostomy, and by the occurrence of homologous serum hepatitis after surgical convalescence.

CASE 1.—A 26-year-old white salesman was admitted to the hospital 45 days after the ingestion of muriatic acid. On that occasion the patient was inebriated and he ingested a small amount of acid in the mistaken belief that it was whiskey. He immediately spat the fluid out, induced vomiting, and then drank a glass of milk. Except for a slight "rawness in the throat," he felt well until the following day when he noted nausea and vomiting after the ingestion of food or liquids. This continued for eight days, and he was hospitalized elsewhere after two episodes of hematemesis. Supportive therapy was instituted with good results, and the patient was discharged without a diagnostic check-up. A similar episode with hospitalization occurred one week later. The third episode of nausea and vomiting without epigastric distress, but this time with dysphagia, occurred four days before admission to the hospital. The patient stated that he had lost 50 lb. (22.7 kg.) in weight in this 45 day period.

The physical examination on admission was essentially negative except for evidence of recent weight loss, moderate dehydration, and tachycardia of 120 beats per minute. The initial hemogram showed only slight leukocytosis with a normal differential count. Urinalysis was essentially negative. Blood chemistry determinations, including non-protein-nitrogen, blood urea nitrogen, blood chlorides, carbon dioxide combining power, and total proteins with the albumin globulin ratio, were within normal limits. Histamine fractional analysis of gastric contents on two occasions failed to show any free hydrochloric acid. The upper gastrointestinal x-ray series, done soon after admission, was reported as follows: "Examination of the esophagus with both thick and thin barium revealed some delay in the passage of the barium through the cardiac sphincter. However, there is no appreciable dilatation of the esophagus. The barium passes into the stomach which does not fill out and repeated attempts to secure filling of the stomach were not successful as the patient was not able to tolerate the barium. Barium remained suspended within what appeared to be the fundus of the stomach; however, there was some slight irregularity in the region of the fundus just above the suspended barium. Radiographs confirm the fluoroscopic findings and reveal a normal esophagus (fig. 1). There is a small amount of barium within the stomach; however, at no time is the barium seen beyond the incisura angularis (fig. 2). Fluoroscopic examination performed at 30 minute intervals revealed no further information. At the end of twenty-four hours, there is a small gastric residue. However, no barium is seen within the small bowel or colon (fig. 3). Impression: Findings suggest a neoplastic lesion involving the pyloric region of the stomach; advise gastroscopy."

Esophagoscopy was done and the esophagus found normal to the cardiac sphincter. Gastroscopy was performed by one of us (M. A. S.). The gastric cavity was found to be very small, holding one cupful of air. The distal portion of the stomach and the fundus were seen practically without moving the instrument, and the mucosa was intact throughout without evident ulceration or scarring. The normal rugal pattern of the stomach was not seen. Cords of tissue covered by epithelium were noted running in various directions. In some areas there was an appearance of webbing, which in some ways mimicked the cardiac chordae tendineae. In the distal portion of the visualized gastric cavity some mucus was seen, and there was a suggestion of an opening into another cavity; however, the gastroscope could not be inserted further. The impression was that there was no tumor. A congenital anomaly of the gastric rugae and mucosa was considered as a possible explanation for the peculiar findings. It was difficult to conceive that a small amount of hydrochloric acid could produce such marked and bizarre changes.

Conservative management failed to relieve the obstruction. An exploratory laparotomy was performed and the following findings noted. The stomach was diffusely thickened and scarred. The distal end of the stomach was entirely obstructed, all mucosal surfaces being in intimate contact. A posterior gastroenterostomy was then performed. A biopsy of the stomach wall, taken during the laparotomy, was later reported as showing chronic inflammation and fibrosis (fig. 4). The patient made an uneventful convalescence and was discharged two weeks later.

This patient was readmitted to the hospital six weeks later with complaints of jaundice of two days duration. This appeared to be a hepatitis of the homologous serum type, which cleared up completely with the standard high protein-high carbohydrate diet bed rest, and added vitamins and lipotropic factors. The patient had received 3 units (900 cc.) of plasma on the day preceding the exploratory laparotomy.

CASE 2.—A 49-year-old white man entered the hospital 46 days after the ingestion of commercial hydrochloric acid (muriatic acid). At that time, the patient had been mentally depressed and despondent about his employment and had ingested the acid with suicidal intent. This was done in the morning before breakfast. Shortly afterwards, he vomited copious amounts of blood, and, several hours later, his stomach was lavaged. Thereafter, his appetite remained poor, with abdominal distention and vomiting occurring after the ingestion of food. There was no dysphagia, and the patient lost over 20 lb. (9.1 kg.) in weight in the following six weeks.

On admission to the hospital, physical examination revealed a depressed, pale, slightly emaciated man whose oral mucous membranes were dry. Blood pressure was 114/80 mm. Hg, and pulse, 80 and regular. The abdomen was scaphoid, and moderate epigastric tenderness was noted. No gastric peristalsis was visible. Throughout this patient's hospital course he ate very little and vomited undigested food several times a day.

The hemogram revealed mild anemia with a red blood cell count of 3,900,000 cells per cubic millimeter and a hemoglobin count of 11.1 gm. (photoelectric colorimeter). Leukocyte count was normal. The blood chlorides, carbon dioxide combining power, urea nitrogen, and fasting sugar were all within normal limits. Total protein was 7.6 gm. per 100 cc., with albumin 3.3 and globulin 4.3 gm. per 100 cc. Liver function tests, including serum bilirubin, total cholesterol and free cholesterol ester ratio, thymol turbidity, thymol flocculation, cephalin-cholesterol flocculation, and alkaline phosphatase were all within

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Published with the approval of the Chief Medical Director, Veterans Administration. The statements and conclusions published by the authors are the results of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

normal limits. Serum potassium was 3.7 mEq. per liter. The upper gastrointestinal x-ray series was reported as follows: "Some fluid was present in the stomach. The antrum and pylorus were narrowed and elongated, producing almost complete obstruction. The narrowing was symmetrical (fig. 5 and 6). At four hours, very little barium had left the stomach. Impression: Infiltrative neoplasm involving the antrum and pylorus." Gastric aspirations 24 hours later revealed barium in the gastric contents in spite of repeated emesis. A histamine fractional gastric analysis failed to reveal any free hydrochloric acid.

Fig. 1 (case 1).—Barium-filled esophagus showing normal caliber and absence of obstruction at cardia.

Subsequently, gastroscopy was performed by one of us (M. A. S.). The instrument was inserted through the esophagus with ease but became arrested in the fundus. Retained food particles were noted. The mucosa was extremely hyperemic and slightly friable. Rugal folds ran radially rather than parallel, suggesting cicatrization. The instrument could not be inserted into the antral region. The impression was a marked superficial gastritis with pyloric obstruction and cascade stomach, or changes in shape due to cicatrization. Because of poor response to conservative therapy, an exploratory laparotomy was done about two weeks after admission. At surgery, cicatrization of the antrum and pylorus were noted. The stomach could not be well mobilized. A posterior gastroenterostomy was performed. The patient had an uneventful convalescence, with rapid gain in weight; however, 50 days after surgery, icterus and a slightly enlarged, tender liver were noted, and a diagnosis of homologous serum hepatitis was made. The patient had received 500 cc. of blood at the time of surgery. Subsequent convalescence was uneventful.

1. Boikan, W. S., and Singer, H. A.: Gastric Sequalae of Corrosive Poisoning, Arch. Int. Med. **46**: 342, 1930.

2. (*a*) Gray, H. K., and Holmes, C. L.: Pyloric Stenosis Caused by Ingestion of Corrosive Substances: Report of a Case, S. Clin. North America **28**: 1041, 1948. (*b*) Gradman, R.; Gerber, S. T., and Kaiser, J.: Corrosive Pyloric Stenosis, Illinois M. J. **100**: 188, 1951.

3. Heindl, D., quoted by Boikan and Singer.[1]

4. Orator, V., quoted by Boikan and Singer.[1] Quenu, quoted by Gray and Holmes.[2a]

5. Vinson, P. P., and Harrington, S. W.: Cicatricial Stricture of the Stomach Without Involvement of the Esophagus Following Ingestion of Formaldehyde, J. A. M. A. **93**: 917 (Sept. 21) 1929.

6. Sick, K., quoted by Boikan and Singer.[1]

COMMENT

The gastric sequalae of corrosive poisoning were fairly well summarized by Boikan and Singer in 1930.[1] It has been pointed out by these workers as well as others [2] that little attention has been paid to this entity in the English literature. Although pyloric stenosis following the ingestion of corrosive acid was described clinically and pathologically about 125 years ago, a recent review [2a] quotes only 3 references in English among a total of 17.

It is well established that alkaline corrosives when swallowed frequently cause extensive necrosis of the esophagus with later cicatricial changes, but because of neutralization in the stomach they cause little damage there; thus, Heindl [3] found that only 20% of 116 cases of esophageal strictures due to lye had associated pyloric stenosis. On the other hand, inorganic acids, in their rapid passage through the esophagus, cause slight damage to this structure, while the prolonged contact with the gastric mucosa due to associated pylorospasm leads to extensive damage to the stomach. Thus, of 86 cases with late pyloric stenosis after acid ingestion,[4] only 20% had associated esophageal stenosis; however, individual reports since these reviews have noted esophageal stenosis in only 2 of 30 cases of late pyloric stenosis (6.5%). Besides the inorganic mineral acids, formaldehyde has been reported to cause gastric stricture without esophageal stenosis,[5] and recently isolated pyloric obstruction secondary to lye ingestion is reported.[2b]

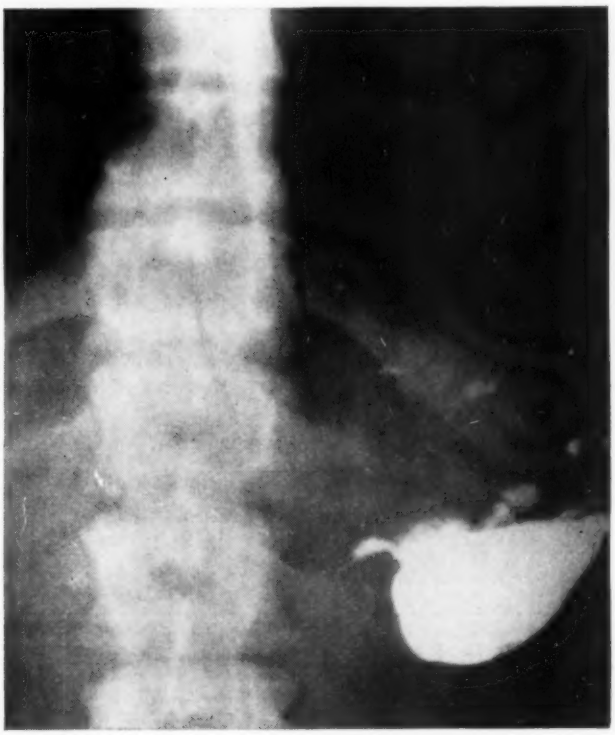

Fig. 2 (case 1).—Roentgenogram of stomach showing antral narrowing and pyloric stenosis.

In the consideration of the factors affecting location and type of gastric lesions produced, not only the type of corrosive ingested but also its concentration are important. The highly concentrated poisons frequently cause perforation and early death. Sick [6] reported a case of

pyloric obstruction following the ingestion of a small amount of dilute acid and, in addition, experimentally demonstrated the importance of a small amount of dilute corrosive in producing extensive gastric damage.

The state of the stomach at the time of corrosive ingestion has been thought to affect the nature of the gastric lesion produced. In a full stomach, the fluid passes quickly to the pylorus, where it is arrested by pylorospasm and spreads out in triangular fashion with the apex toward the cardia and the base ending just proximal to the pyloric ring. This pathological picture was noted in one of Boikan and Singer's cases at autopsy two weeks after the ingestion of dilute lye. If the validity of the "magenstrasse" is accepted, then the corrosive contacts the lesser curvature and pyloric mucosa on the one side and the diluting effects of food and/or liquid on the other. Emesis then leaves a raw ulcerated lesser curvature and pars pylorica. On the other hand, in the empty contracted stomach in which the lesser curvature tends to attain a vertical position, the corrosive contacts the entire mucosa with longest contact in the pars pylorica and media. In this situation, the corrosive is bordered by mucosa of a spastic pylorus distally and the fundic air, above the fluid, proximally. Thus here, late sequalae are

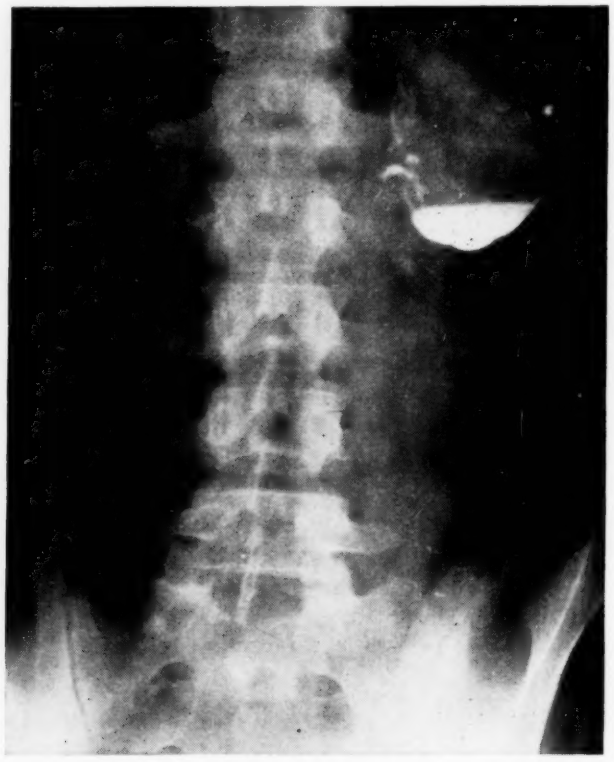

Fig. 3 (case 1).—Roentgenogram of stomach 24 hours after ingestion of barium meal still showing retention.

pyloroantral constriction with simultaneous narrowing of the pars pylorica and pars media or total gastric scarring (linitis plastica type), or hourglass stenosis due to antral constriction. In both instances, the prepyloric area carries the brunt of the damage. We feel that the first of our cases (case 1) probably represents the "linitis plastica" type of total gastric scarring, and the second (case 2) is an example of the pyloroantral constriction type; however, the types of lesions found in our patients tend to refute the accepted relation between gastric content and resultant gastric damage. Patient 1 had been on a drinking spree at the time of corrosive ingestion, and his stomach had been, presumably, at least partially full, and yet the lesion was diffuse. It might be explained that the induced emesis produced contact between the corrosive and the mucosa of the upper half of the stomach with the production of the diffuse scarring as noted later at laparotomy. Patient 2 ingested the corrosive in the morning before breakfast on a presumably empty stomach, and the cicatrization was chiefly antral and pyloric.

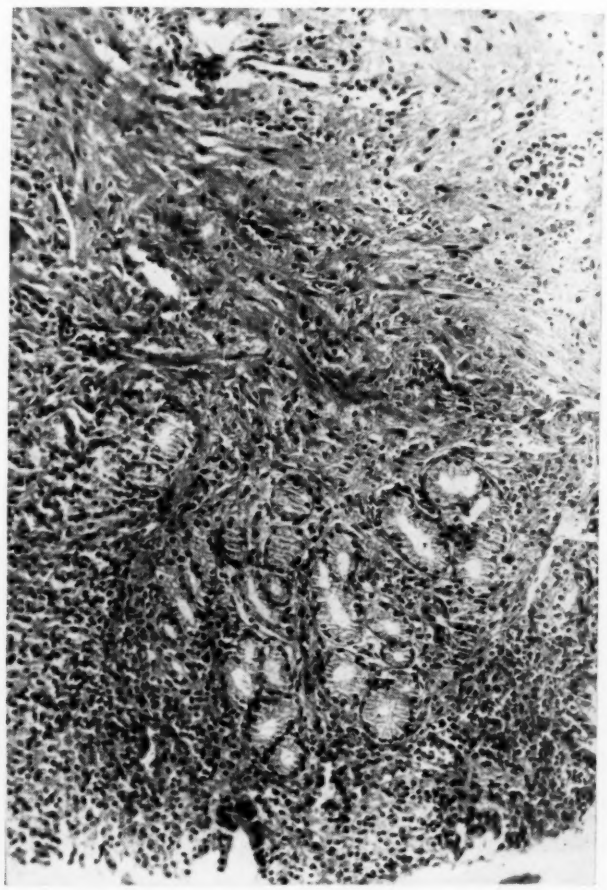

Fig. 4 (case 1).—Biopsy of stomach wall showing fibrosis and round cell infiltration.

In addition to stenotic lesions, other sequalae ascribed to hydrochloric acid ingestion are acute corrosive gastritis and acute emphysematous gastritis.[7] Both Schindler [8] and Palmer [9] have described the gastroscopic picture of acute corrosive gastritis with subsequent return of a normal gastroscopic picture. The latter author noted the return of a gastroscopically normal stomach by the 55th day and felt that this type of evidence refuted the idea of a "magenstrasse." He explained the late pyloric involvement on the basis of "the greater susceptibility of the antral region to noxious influences" rather than on the basis of greatest concentration of corrosive.

7. Weems, H. S.: Emphysematous Gastritis, Am. J. Roentgenol. **55**: 588, 1946.

8. Schindler, R.: Gastritis, New York, Grune & Stratton, Inc., 1947, p. 443.

9. Palmer, E. D., and Scott, N. M., Jr.: Acute Corrosive Gastritis: Observations on the Gastric Mucosa Following Ingestion of Concentrated Hydrochloric Acid, Gastroenterology **12**: 879, 1949.

In the English literature, Putnam [10] reported a case of pyloric excision for stricture secondary to acid ingestion in 1915. McLanahan [11] in 1934 and Arena [12] in 1936 reported cases of pyloric obstruction following muriatic acid ingestion. In these cases, as in ours, the pyloric stenosis became markedly symptomatic in 3 to 6 weeks. Boikan and Singer [1] felt that late gastric stenosis should be anticipated in all cases of corrosive ingestion, particularly with acids. Schulenburg [13] reported a case and based his conclusions for local damage on the experimental work of Testa with barium-caustic soda studies in dogs.

In the convalescent course of both the patients reported, hepatitis, presumably of the homologous serum type, was discovered about six weeks postoperatively. Neither patient had any previous evidence of gross liver damage, although the blood globulin concentration in case 2 was slightly elevated. In both cases, the disease process was relatively mild, and both patients recovered without residua. One may speculate about the possible explanations for the hepatitis in both of these cases. The patients were treated in different hospitals but received blood and plasma from the same bank. The first patient received one blood transfusion of 500 cc. The following

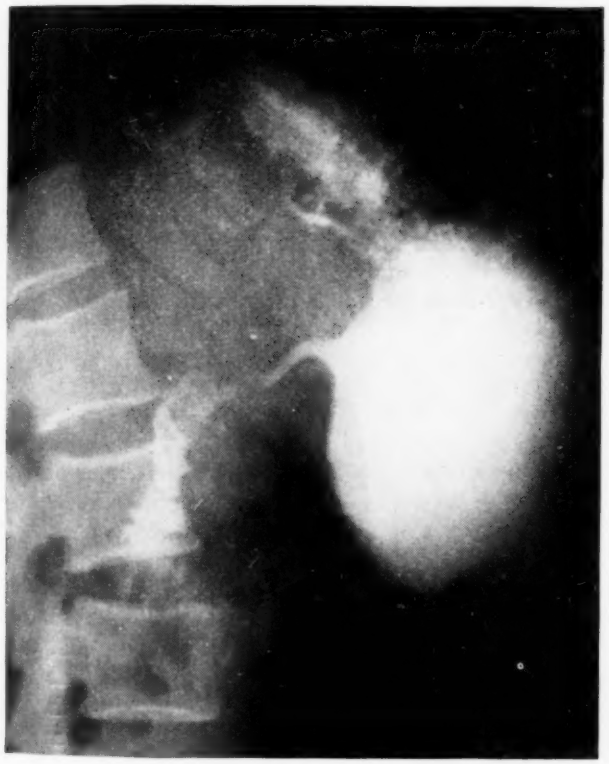

Fig. 5 (case 2).—Roentgenogram of stomach showing marked contraction of antrum and pyloric stenosis.

possibilities exist. 1. It was entirely coincidental that hepatitis developed in both of these patients with the same illness. 2. The lowered resistance and malnutrition of these persons made them an easy prey to this infection. 3. The specific damage and extensive erosions of the gastric mucosa may predispose to viral hepatitis. 4. This particular type of gastric injury may result in hepatitis independent of the use of blood or plasma. While the last two possibilities are highly speculative, this complication should be anticipated and reported in the future to further elucidate these points.

TREATMENT

Therapy during the acute phase is supportive, including measures to combat infection, hemorrhage, and/or shock. Neutralization with bicarbonate or other gas re-

Fig. 6 (case 2).—Roentgenogram of stomach six hours after ingestion of barium showing practically no emptying.

leasing substances should be avoided. Lavage should be undertaken with extreme caution because of a tendency of the stomach to perforate. Elisher [14] noted that perforation and collapse was less frequent after hydrochloric acid ingestion than after sulfuric acid ingestion. Fluid balance and nutrition should be maintained by parenteral fluid and blood transfusions. The latter should not be used indiscriminately in view of the hepatitis noted in our two cases. Meyer and Steigmann [15] emphasized the edema and friability of the stomach during the acute phase, precluding suturing of the gastric wall. The recommended jejunostomy at this stage if necessary.

Later therapy is directed toward the late sequelae, i. e., pyloric obstruction. Gray and Holmes [2a] recommended partial gastrectomy in young patients in view of the possibility of malignant degeneration, stomal ulcer for-

10. Putnam, C. R. L.: Excision of the Pylorus for Stricture due to the Ingestion of an Acid, M. Rec. **87**: 332, 1915.
11. McLanahan, S.: Pyloric Occlusion Following the Ingestion of Corrosive Liquids, J. A. M. A. **102**: 735 (March 10) 1934.
12. Arena, J. M.: Pyloric Stricture Following Ingestion of Muriatic Acid, South. M. J. **29**: 331, 1936.
13. Schulenburg, C. A. R.: Corrosive Stricture of Stomach Without Involvement of Oesophagus, Lancet **2**: 367, 1941.
14. Elisher, E., quoted by Gray and Holmes.[2a]
15. Meyer, K. A., and Steigmann, F.: The Surgical Treatment of Corrosive Gastritis, Surg., Gynec. & Obst. **79**: 306, 1944.

mation, and/or the difficulty of accomplishing satisfactory gastroenterostomy. The last mentioned would seem most plausible while the former two are merely conjectural. Gradman and his colleagues feel that gastroenterostomy is the simplest and safest procedure, providing that the gastric wall at the anastomotic site is normal. We agree with this completely. In our two cases posterior gastrojejunostomy yielded excellent results. If a direct anastomosis is not feasible, then the procedure of choice is a subtotal gastric resection.

SUMMARY

Two cases of stenotic gastric lesions without esophageal involvement secondary to commercial hydrochloric acid ingestion are reported, and attention is called to the paucity of such reports in the English literature.

The relation of the quantity of gastric contents to the type and nature of gastric lesions produced is discussed, and the occurrence of postoperative hepatitis in both cases is noted.

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SIMULTANEOUS INDEPENDENT PAROXYSMAL TACHYCARDIAS

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The occurrence of simultaneous independent paroxysmal tachycardias is regarded as extremely rare. It is not known, however, whether the incidence of double tachycardias is really low or only apparently so, owing to the difficulty of diagnosis because of superimposition of auricular complexes at a rapid rate on ventricular complexes. In a recent study at the Cook County Hospital we have encountered seven cases of dissociated paroxysmal tachycardias during a 10 month period. In six instances there was a paroxysmal ventricular tachycardia with a simultaneous independent paroxysmal supraventricular pacemaker. Of the supraventricular mechanisms, two were auricular tachycardia and four were auricular flutter. In the seventh case dissociated paroxysmal auricular and nodal tachycardias were present.

The occurrence of auricular fibrillation with ventricular tachycardia is not infrequent, but the incidence of auricular paroxysmal tachycardia or auricular flutter with ventricular (or nodal) tachycardia is rare. In 1930 Strauss,[1] reviewing the literature, found 65 cases of ventricular tachycardia, of which 21 had auricular fibrillation. Hepburn and Rykert [2] described two cases among 26 patients with ventricular tachycardia that occurred during quinidine therapy for auricular fibrillation. Williams and Ellis [3] found auricular fibrillation present in 14 of 36 cases of ventricular tachycardia. Herrmann and Hejtmancik [4] added four instances of this combination in 20 cases. In 1950 Armbrust and Levine [5] reported auricular fibrillation in 20 of 107 cases of ventricular tachycardia. The auricular mechanisms immediately following termination of the ventricular paroxysmal tachycardias were not recorded in the cases of Lundy and McLellan,[6] Scherf and Kisch,[7] and Cooke and White.[8] The great frequency of auricular fibrillation in cases of paroxysmal ventricular tachycardia is not surprising, since either arrhythmia may be related to coronary artery disease. In most instances the auricular fibrillation was chronic. In 2 of the 14 cases of Williams and Ellis,[3] however, the auricular fibrillation was paroxysmal, reverting spontaneously to sinus mechanism within two weeks.

In contrast to the frequency of auricular fibrillation plus paroxysmal ventricular tachycardia, the combination of auricular flutter and paroxysmal ventricular tachycardia appears to be extremely rare. Gallavardin [9] in 1920 reported one such case. In 1932 McMillan and Bellet [10] referred to two instances of ventricular tachycardia in 65 cases of auricular flutter. Recently reporting on 15 cases of paroxysmal ventricular tachycardia, Kayden and co-workers [11] found auricular flutter after the cessation of paroxysmal ventricular tachycardia in one instance. In 1937 Stern [12] described a case of auricular flutter and a regular rapid ventricular rhythm that was diagnosed as a ventricular tachycardia. He made the diagnosis of ventricular tachycardia because of a change in shape of the QRS complex occurring with termination of the tachycardia, although the QRS duration was less than 0.12 second. We believe that these complexes represented a nodal tachycardia and that the observed change in QRS contour was due either to aberrant conduction or to change of heart position during the tachycardia. No other examples of this combination have been found in the literature.

The combination of paroxysmal auricular tachycardia and ventricular or nodal tachycardia also appears to be rare. In 1924 Barker [13] reported a case of paroxysmal auricular tachycardia that became obscured by a parox-

Dr. Richard Langendorf assisted in the interpretation of the electrocardiograms and in the preparation of this paper.

The procaine amide hydrochloride ("pronestyl") used in this study was supplied by E. R. Squibb & Sons, New York.

The acetyl strophanthidin used in this study was supplied by Eli Lilly & Company, Indianapolis.

From the Department of Medicine, Cook County Hospital, the Departments of Clinical Science and Medicine, University of Illinois College of Medicine, and the Department of Medicine, Stritch School of Medicine, Loyola University.

1. Strauss, M. B.: Paroxysmal Ventricular Tachycardia, Am. J. M. Sc. **179**: 337, 1930.

2. Hepburn, J., and Rykert, H. E.: The Use of Quinidine Sulfate Intravenously in Ventricular Tachycardia, Am. Heart J. **14**: 620, 1937.

3. Williams, C., and Ellis, L. B.: Ventricular Tachycardia: An Analysis of 36 Cases, Arch. Int. Med. **71**: 137 (Feb.) 1943.

4. Herrmann, G. R., and Hejtmancik, M. R.: A Clinical and Electrocardiographic Study of Paroxysmal Ventricular Tachycardia and Its Management, Ann. Int. Med. **28**: 989, 1948.

5. Armbrust, C. A., Jr., and Levine, S. A.: Paroxysmal Ventricular Tachycardia: A Study of 107 Cases, Circulation **1**: 28, 1950.

6. Lundy, C. J., and McLellan, L. L.: Paroxysmal Ventricular Tachycardia: An Etiological Study with Special Reference to the Type, Ann. Int. Med. **7**: 812, 1943.

7. Scherf, D., and Kisch, F.: Ventricular Tachycardias with Variform Ventricular Complexes, Bull. New York M. Coll., Flower & Fifth Ave. Hosps. **2**: 73, 1939.

8. Cooke, W. T., and White, P. D.: Paroxysmal Ventricular Tachycardia, Brit. Heart J. **5**: 33, 1943.

ysm of ventricular tachycardia. The following year Luten [14] described two cases of simultaneous auricular and nodal tachycardias. In 1927 Howard [15] recorded an additional case with the latter combination. We have found no additional cases of this kind. The accompanying table summarizes the reported cases of double tachycardias.

DIAGNOSIS OF DOUBLE TACHYCARDIAS

The diagnosis of double tachycardias presents two main problems. The first is the technical difficulty of recognizing the auricular waves, which may be obscured by the rapid, broad, slurred QRS complexes of the ventricular tachycardia; and the second is the difficulty of accepting the tachycardia as being conclusively ventricular (or nodal) in origin in the presence of an auricular rate greater than that of the ventricles. The F waves of auricular fibrillation are not discernible in the presence of ventricular tachycardia. Indeed, the presence of auricular fibrillation during paroxysms of ventricular tachycardia is inferred only from its presence prior to and immediately following termination of the ventricular paroxysms. Similarly, the F waves of auricular flutter, which are usually (but not invariably) obscured by the rapid, broad, erratic QRS complexes of the ventricular tachycardia, are also inferred to have been present during the ventricular paroxysmal tachycardia. In contrast, the P waves of paroxysmal auricular tachycardia may be of low enough frequency and of sufficient amplitude as to be clearly evident when superimposed upon the QRS complexes of a ventricular tachycardia. In nodal tachycardia, because the QRS complexes are narrower, the waves of independent auricular activity are obscured much less than in ventricular tachycardia.

Having accepted the presence of a rapid auricular mechanism, either inferentially or by identifying F or P waves, the relationship of ventricular activation to the rapid auricular impulses must be evaluated. It is known that ventricular tachycardia may be simulated by aberrant conduction within the ventricle of rapidly transmitted impulses from auricular tachycardia, auricular flutter, or auricular fibrillation. Hence, an important criterion for the diagnosis of ventricular tachycardia has been the recognition of auricular P waves at a rate slower than that of the ventricles. If a paroxysmal rapid regular auricular rate is less than the rapid ventricular rate, the independence of the two tachycardias is established. In such a case, if the QRS complex is of normal duration, the other tachycardia is said to be of A-V nodal origin. If the QRS is prolonged, the pacemaker is either in the ventricle or in the A-V node, with aberrant intraventricular conduction.

The differentiation of ventricular tachycardia from nodal tachycardia with aberrant conduction can seldom be made with certainty. Thus, in this paper the diagnosis of ventricular tachycardia is not intended to exclude the possibility of nodal tachycardia with aberrant conduction. The dependence of a regular, rapid auricular rate resulting from 1:1 retrograde conduction of a regular nodal or ventricular tachycardia can be recognized by the constant relationship of the P waves to the QRS complexes. A rapid auricular rate resulting from retrograde conduction with second degree block can be differentiated from an independent paroxysmal auricular tachycardia by the irregularity of the P waves. If the auricular paroxysmal rate is greater than the ventricular paroxysmal rate, conclusive demonstration of the ventricular origin of the supposed paroxysmal ventricular tachycardia may not be possible, since aberrant conduction of rapidly transmitted auricular impulses cannot be excluded. Combinations of fixed or varying A-V conduction ratios and fixed or varying A-V conduction rates in the presence of aberrant conduction may simulate either regular or irregular ventricular tachycardias.

It should be emphasized that in the four cases presented here as combinations of independent paroxysmal ventricular tachycardia and auricular flutter, the diagnosis is not unequivocal. There is no way to definitely exclude aberrant ventricular conduction of rapidly transmitted auricular impulses. The presence of auricular fibrillation immediately after cessation of a supposed ventricular tachycardia has been offered as a criterion supporting the latter mechanism because it was believed to exclude paroxysmal supraventricular tachycardia with 1:1 aberrant conduction. The auricular fibrillation is assumed to have been present and independent of the paroxysm of ventricular tachycardia. The same assumptions would seem to apply in instances in which auricular flutter is found after termination of paroxysmal ventricular tachycardia and in which there is no clear relationship between the rates of the auricular flutter and ventricular tachycardia. In cases in which the auricular rate is greater than that of the ventricles, but within the range of paroxysmal auricular tachycardia, perfectly regular ventricular and auricular rates may be seen to be entirely independent. If the ventricular mechanism is irregular, independence of the auricular and ventricular mechanisms cannot be established; however, the demonstration of change of auricular mechanism without alteration of the ventricular mechanism is proof of the nodal or ventricular origin of the ventricular rhythm. Such a no-

Summary of Reported Cases of Double Tachycardias Found in the Literature

	Year	Ventricular and Auricular Tachycardias	Ventricular Tachycardia and Auricular Flutter	Nodal and Auricular Tachycardias	Nodal Tachycardia and Auricular Flutter
Gallavardin [9]	1920	..	1	..	..
Barker [13]	1924	1	..	..	..
Luten [14]	1925	2	..	1	..
Howard [15]	1927	..	..	1	..
McMillan and Bellet [10]	1932	..	2	..	..
Stern [12]	1937	..	..	..	1
Kayden et al. [11]	1951	..	1	..	..
Totals		3	4	2	1

9. Gallavardin, L.: Tachycardie ventriculaire terminale greffée sur une tachysystolie auriculaire, Arch. d. mal. du coeur **13**: 210, 1920.

10. McMillan, T. M., and Bellet, S.: Auricular Flutter: Some of Its Clinical Manifestations and Its Treatment: Based on a Study of 26 Cases, Am. J. M. Sc. **184**: 33, 1932.

11. Kayden, H. J.; Steele, J. M.; Mark, L. C., and Brodie, B. B.: The Use of Procaine Amide in Cardiac Arrhythmias, Circulation **4**: 13, 1951.

12. Stern, N. S.: Paroxysmal Ventricular Tachycardia: Report of 3 Cases: Mecholyl Used and Ineffective in 2, Ann. Int. Med. **11**: 519, 1937.

13. Barker, P. S.; Macleod, A. C., and Alexander, J.: The Excitatory Process Observed in the Exposed Human Heart, Am. Heart J. **5**: 720, 1930.

14. Luten, D.: Clinical Studies of Digitalis: Toxic Rhythms with Special Reference to the Similarity Between Such Rhythms in Man and in the Cat, Arch. Int. Med. **35**: 74 (Jan.) 1925; Advanced Toxic Rhythms, ibid. **35**: 87 (Jan.) 1925.

15. Howard, T.: Double Tachycardia: Coexistent Auricular and Ventricular Tachycardia Due to Digitalis, Am. J. M. Sc. **173**: 165, 1927.

ticeable change in auricular mechanism is usually to that of a sinus rhythm at a rate less than the ventricular rate, which further confirms the nodal or ventricular origin of ventricular activation.

Of the seven cases of simultaneous dissociated paroxysmal tachycardias presented here, the diagnosis is unequivocal in three (all having paroxysmal auricular tachycardia) and inferential in four (all having auricular flutter). In some instances therapy was started by house officers before the patients were seen by the authors, in whose judgment, incidentally, this initial treatment was thought to be inappropriate.

REPORT OF CASES

CASE 1.—The patient was a 50-year-old white man with a history of anterior myocardial infarction on his first admission in June, 1949. This diagnosis was substantiated by serial electrocardiograms. At that time paroxysmal ventricular tachycardia occurred and was converted to sinus rhythm with orally administered quinidine. During the following 15 months, while the patient was receiving maintenance doses of quinidine, several episodes of ventricular tachycardia occurred, each being converted with quinidine given orally. On Sept. 6, 1950, he was admitted because of recurrent proxysmal tachycardia and was treated with procaine amide hydrochloride ("pronestyl").

Lead V_1 of the electrocardiogram taken at the time of the patient's admission (fig. 1,*A*) revealed two independent pacemakers, one auricular, the other ventricular. The auricular paroxysmal focus gave rise to upright P waves at a rate of 142 per minute. In this patient, P waves of sinus origin were negative in lead V_1, as seen in figure 1,*D*; hence, the upright P waves indicated an ectopic focus. The paroxysmal ventricular tachycardia, at a rate of 146, arose from a left ventricular focus and had alternating R-R intervals of different duration. No auricular impulses were transmitted to the ventricles. During the intravenous administration of procaine amide hydrochloride, the auricular rate slowed gradually from 142 to 124; and after a total dose of 500 mg. of the drug had been given, the auricles converted to a sinus mechanism at a rate of 68 (fig. 1,*B*). Meanwhile, the ventricular tachycardia had gradually slowed from 146 to 135, but conversion of the paroxysmal auricular tachycardia was without effect upon the ventricles, further demonstrating the complete independence of the two paroxysmal mechanisms. Continued intravenous administration of procaine amide hydrochloride gradually slowed the ventricular tachycardia to a rate of 112 (at a total drug dose of 1,300 mg.), with an independent sinus mechanism at a rate of 79 (fig. 1,*C*). After 1,400 mg. of the drug had been administered, and during a 30 second interval between strips *C* and *D* of figure 1 (at which time the electrocardiogram was not being recorded), conversion of the ventricular tachycardia to sinus mechanism occurred. Figure 1,*D*, immediately after conversion, reveals P waves similar in contour and rate to the P waves in strip *C*, with conduction to and activation of the ventricles, resulting in QRS complexes of normal contour and duration.

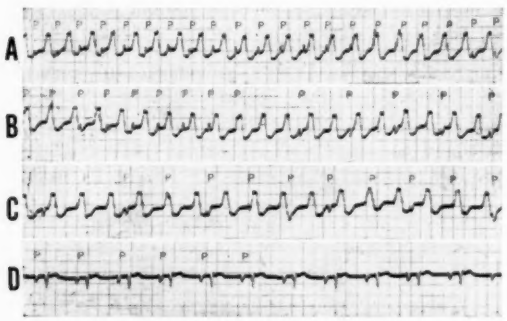

Fig. 1 (case 1, lead V_1).—*A*, paroxysmal auricular tachycardia, rate 142, and paroxysmal ventricular tachycardia, rate 146, totally dissociated. There are alternating R-R intervals of different duration. *B*, conversion of paroxysmal auricular tachycardia without change of ventricular tachycardia after administration of 500 mg. of procaine amide hydrochloride ("pronestyl"). Note change of inverted (positive) P waves at a rate of 124 to sinus (negative) P waves at a rate of 68. *C*, ventricular tachycardia slowed to a rate of 112 after administration of 1,300 mg. of procaine amide hydrochloride, immediately preceding its conversion. Sinus auricular mechanism persists. *D*, normal sinus mechanism, rate 80, immediately following conversion of ventricular tachycardia after administration of 1,400 mg. of procaine amide hydrochloride.

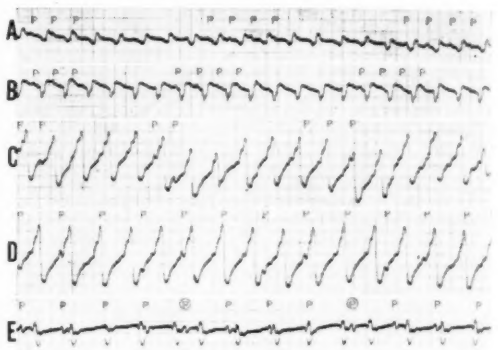

Fig. 2 (case 2).—*A*, standard lead I. Ventricular tachycardia, rate 135, with independent paroxysmal auricular mechanism, rate 150. *B*, lead V_1. Same as *A*, revealing P waves at identical rate. The ventricular ectopic focus is in the right ventricle. *C*, lead V_1. The ventricular ectopic focus has changed from the right to the left ventricle and slowed to 118 after administration of 100 mg. of procaine amide hydrochloride ("pronestyl"). The auricular mechanism has slowed to 145. *D*, lead V_1. The ventricular tachycardia slowed to 105 after administration of 200 mg. of procaine amide hydrochloride. The paroxysmal auricular mechanism has been converted to a sinus mechanism, rate 80. *E*, lead V_1. After administration of 1,500 mg. of procaine amide hydrochloride, there is sinus auricular mechanism, rate 80, identical with that in *D*, nodal tachycardia with right bundle branch block, and interference with intermittent dissociation. Auricular impulses signified by encircled P waves are conducted, being followed by premature ventricular complexes. These are instances of "ventricular capture."

Summary of Case.—Simultaneous completely dissociated paroxysmal auricular and ventricular tachycardias were demonstrated by conversion of the paroxysmal auricular to a sinus mechanism without changing the ventricular mechanism. Subsequently the ventricular tachycardia was terminated.

CASE 2.—The patient was a 65-year-old white man with a history of dyspnea and leg edema for one year. He was admitted three days after an episode of severe, crushing substernal pain that radiated to the left arm. There were moist rales in both lower lung fields and a moderate pitting edema of the sacral region and lower extremities. The liver was enlarged and tender. The apical rate was 112; blood pressure, 90/45 mm. Hg. The patient was treated with morphine, oxygen, meralluride injection (mercuhydrin® sodium solution) and 1.2 mg. of digitoxin given orally. His general condition was very poor. The following morning he was found to have a slightly irregular apical rate of 130 to 140.

An electrocardiogram at that time showed a ventricular tachycardia. There was an independent auricular mechanism at a rate of 150. Strips of this record are shown to demonstrate the P waves in two leads, leads I (fig. 2,*A*) and V_1 (fig. 2,*B*). In both strips the auricular rate was 150. After 100 mg. of procaine amide hydrochloride was administered intravenously, an ectopic focus in the left ventricle replaced that in the right ventricle, as shown by the change in QRS contour in lead V_1 from negative to positive (fig. 2,*C*). The ventricular rate had slowed to 118, and the auricular rate had slowed slightly. After a total drug dose of 200 mg. was given, the paroxysmal auricular mechanism converted to a sinus mechanism at a rate of 80, and the ventricular tachycardia was further slowed to 105 (fig. 2,*D*). Changes in contour of the P waves were not definite enough to aid in making the diagnosis of paroxysmal auricular tachycardia; however, the sudden change in P wave rate from 145 to 80 justifies this diagnosis rather than the diagnosis of sinus tachycardia. After a total administration of 1,500 mg. of procaine amide hydrochloride, a conversion of the ventricular

tachycardia to a nodal tachycardia with right bundle branch block occurred, with interference and intermittent dissociation (fig. 2,*E*). In this lead the auricular impulses signified by encircled P waves are conducted through the node, resulting in ventricular captures. No other auricular impulses are conducted, because they arrived at the node during the refractory phase following the impulses originating in the node. Intravenous administration of a total dose of 4 gm. of procaine amide hydrochloride during a two hour period slowed the nodal rhythm to 90 but failed to convert it to a sinus mechanism. Maintenance doses of procaine amide hydrochloride were then given orally. The patient became progressively worse and expired two days later. Acute myocardial infarction in the presence of arteriosclerotic heart disease was the clinical diagnosis. An autopsy was not performed.

Summary of Case.—Simultaneous dissociated paroxysmal auricular and ventricular tachycardias were demonstrated. Conversion of the paroxysmal auricular tachycardia to a sinus mechanism occurred without conversion of the ventricular tachycardia. The administration of additional doses of procaine amide hydrochloride gradually slowed the ventricular pacemaker, shifted the ectopic focus from the right to the left ventricle, and, finally, converted ventricular tachycardia to nodal tachycardia and bundle branch block with occasional ventricular capture.

Case 3.—The patient was an 80-year-old Negro woman with a history of several years of dyspnea, orthopnea, and edema of the lower extremities, who had been treated adequately with digitalis, a low sodium chloride diet, and mercurial diuretics. She was readmitted because of severe progression of her symptoms. An electrocardiogram made at the time of her admission revealed a sinus rhythm at a rate of 80. She failed to respond to usual therapy, became progressively more decompensated, then comatose. An electrocardiogram at that time (fig. 3,*A*) showed an auricular rate of 190 and a regular ventricular rate of 118. The QRS duration was not prolonged. No constant relationship of the P waves to the QRS complexes was found; hence, the diagnosis of dissociated paroxysmal auricular and nodal tachycardias was made. After 100 mg. of procaine amide hydrochloride had been given intravenously, the auricular tachycardia was converted to a sinus mechanism at a rate of 75 (fig. 3,*B*) without affecting the ventricular response to the nodal pacemaker, which had been slowed to 112. Complete dissociation existed for four minutes. Without additional administration

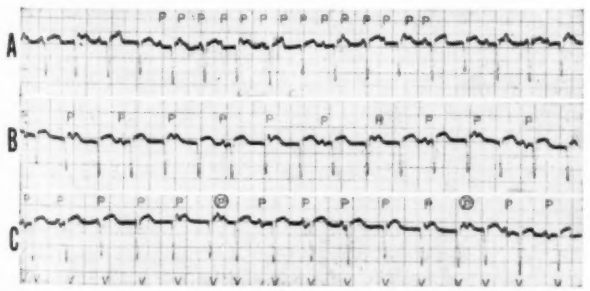

Fig. 3 (case 3, lead V_1).—*A*, paroxysmal auricular tachycardia, rate 190, and nodal tachycardia, rate 118, completely dissociated. *B*, sinus auricular mechanism, rate 75, complete A-V dissociation, and nodal tachycardia, rate 112, after administration of 100 mg. of procaine amide hydrochloride ("pronestyl"). *C*, interference and intermittent dissociation is present. Slowing of nodal pacemaker to 92 allows occasional auricular impulse (encircled P waves) to be conducted to and activate the ventricles prematurely.

of procaine amide hydrochloride, further slowing of the nodal pacemaker to 105 allowed occasional transmission of auricular impulses and ventricular captures (fig. 3,*C*). A total dosage of 1,600 mg. of procaine amide hydrochloride further slowed the nodal pacemaker without change in the mechanism. The patient expired two days later. Autopsy revealed coronary sclerosis and diffuse myocardial fibrosis.

Summary of Case.—Simultaneous dissociated paroxysmal auricular and nodal tachycardia were demonstrated. Conversion of the auricular tachycardia to sinus rhythm without change of the nodal tachycardia substantiated this diagnosis. Nodal slowing allowed occasional ventricular capture. Conversion of the nodal rhythm did not occur.

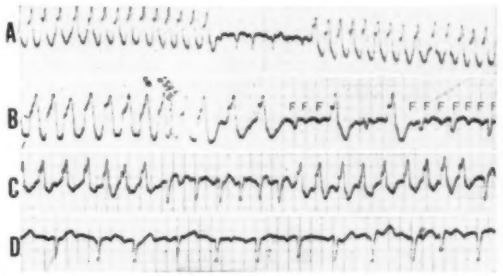

Fig. 4 (case 4, lead V_1).—*A*, alternating runs of paroxysmal ventricular tachycardia, originating in the left ventricle, and irregularly conducted beats of left bundle branch block pattern. *B*, slowing, then suppression of the paroxysmal ventricular tachycardia after administration of 200 mg. of procaine amide hydrochloride ("pronestyl"). Auricular flutter with decreased varying A-V conduction and frequent left ventricular ectopic beats. The electrocardiograph was stopped momentarily in this strip. *C*, recurrence of short paroxysms of ventricular tachycardia following the administration of acetyl strophanthidin. *D*, complete suppression of ectopic ventricular activity following an additional administration of 1,200 mg. of procaine amide hydrochloride.

Case 4.—The patient was a 70-year-old white man admitted with severe dyspnea, orthopnea, cyanosis, palpitation, and intermittent substernal pain of several hours' duration. There was 3+ pitting edema of the lower extremities and over the sacrum. The liver was palpable 4 cm. below the costal margin and was slightly tender. The heart rhythm was irregular at a rate of about 240; blood pressure was 95/70 mm. Hg. The patient had been attending the cardiac clinic since an admission two years previously and had been well compensated, receiving digitalis and weekly mercurial injections. It was not known until later that an electrocardiogram at the time of his previous admission showed an auricular flutter with 4:1 conduction.

An electrocardiogram taken shortly after the patient's latest admission showed alternating runs of two distinct types of tachycardia. One type was of slightly irregular rhythm, with wide, aberrant QRS complexes of right bundle branch block pattern at a rate of about 240. This condition alternated with short runs of grossly irregular rhythm, with QRS complexes resembling those of the left bundle branch block at a rate of about 180 (fig. 4,*A*). A presumptive diagnosis was made of paroxysms of ventricular tachycardia, possibly originating from more than one focus. Following the intravenous administration of 200 mg. of procaine amide hydrochloride, the paroxysms of tachycardia of right bundle branch block contour were suppressed. This revealed the presence of an auricular flutter (rate 240) with varying A-V conduction, resulting in an irregular ventricular response of left bundle branch block pattern at a rate of 90 to 110 and occasional single QRS complexes of right bundle branch block contour (fig. 4,*B*). The left bundle branch block QRS complexes in the slower of the two types of paroxysms noted before treatment were the same as those remaining after slowing of the ventricular response to 90. It was thus concluded that the slower, grossly irregular tachycardia with QRS complexes of an LBBB pattern was an irregular response to conducted auricular impulses. Because of the recognition of an auricular rate faster than that of the suppressed paroxysms of tachycardia of RBBB contour, it was erroneously assumed that those runs were also transmitted auricular impulses, the conduction of which was aberrant when the ventricular response was extremely rapid.

A digitalis preparation was believed indicated in order to maintain a high degree of A-V block. Three units of acetyl strophanthidin were administered intravenously over a 10 minute period and repeated 45 minutes later. Following this there recurred the two types of paroxysms of tachycardia present at

the time of the patient's admission (fig. 4,*C*). Intravenous administration of procaine amide hydrochloride was then repeated. A total of 1,200 mg. caused gradual slowing, then suppression, of the paroxysms of tachycardia with QRS complexes of right bundle branch block pattern. Auricular flutter persisted with an irregular ventricular response at a rate of 85 to 95 (fig. 4,*D*). On retrospection it was concluded that the gradual slowing, then suppression, of the right bundle branch block pattern paroxysms by administration of procaine amide hydrochloride and the reinstitution of this tachycardia by a digitalis preparation indicated that these runs were truly paroxysmal ventricular tachycardia; but final differentiation from aberrant conduction of rapidly transmitted auricular impulses could not be made.

In spite of the administration of oxygen, morphine, mercurial diuretics, and the maintenance of a slow ventricular rate by orally administered procaine amide hydrochloride, the patient's condition deteriorated, and death occurred two days later. The clinical diagnosis was arteriosclerotic heart disease. A postmortem examination was not made.

Summary of Case.—Short paroxysms of ventricular tachycardia were suppressed by the intravenous administration of procaine amide hydrochloride. Between and after the paroxysms of ventricular tachycardia, auricular flutter with varying A-V conduction was demonstrated. It was assumed that the auricular flutter was present during the paroxysms of ventricular tachycardia, with no

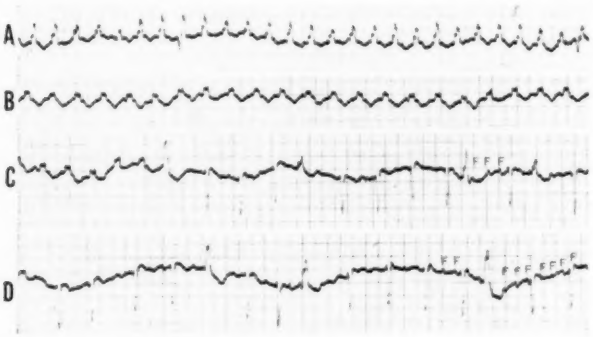

Fig. 5 (case 5, lead V_2).—*A*, paroxysmal ventricular tachycardia, rate 178. *B*, slowing of paroxysmal ventricular tachycardia to 147, with widening of QRS complexes after administration of 400 mg. of procaine amide hydrochloride ("pronestyl"). *C*, termination of the paroxysmal ventricular tachycardia occurring five seconds after the end of strip *B*, following administration of 400 mg. of procaine amide hydrochloride. Auricular flutter waves discernible. *D*, additional graph after termination of the ventricular tachycardia, demonstrating auricular flutter with varying A-V conduction and frequent ventricular ectopic beats.

transmission of auricular impulses occurring. The erroneous interpretation of the runs of ventricular tachycardia as aberrant conduction of rapidly conducted impulses from the auricular flutter led to strophanthidin therapy and a recurrence of the paroxysmal ventricular tachycardia.

CASE 5.—The patient was an 80-year-old colored man admitted in a confused state. He was severely dyspneic and cyanotic and expectorated pink, frothy sputum. There were moist rales in both lower lung fields and coarse rhonchi throughout. The neck veins were distended; the liver was palpable 6 cm. below the costal margin; and there was moderate pitting edema over the sacrum and lower extremities. No popliteal or dorsal pedal pulse could be discerned on the right foot, which was cold and cyanotic. The heart was greatly enlarged. The apical rate was 130, irregular; radial pulse, 90, irregular; blood pressure, 162/100 mm. Hg. Therapy consisted of oxygen, morphine, mercurial diuretics, and digitalis preparations. Initially the patient was given two ampules of digalen® intravenously and 0.8 mg. of digitoxin orally. Within six hours he received an additional 0.4 mg. of digitoxin and 4 cc. of digalen.® During this period the apical rate remained between 135 and 150 and was irregular. Eight hours after the patient was admitted, his apical rate was found to be 176, regular. Blood pressure was 150/110 mm. Hg. An electrocardiogram taken at that time revealed a paroxysmal ventricular tachycardia (fig. 5,*A*). Administration intravenously of 400 mg. of procaine amide hydrochloride slowed, then terminated, the paroxsymal tachycardia (fig. 5,*B* and *C*). Following suppression of the paroxysmal tachycardia, F waves of an auricular flutter with varying A-V conduction were found (fig. 5,*D*). The auricular flutter was assumed to have been present before and during the paroxysm of ventricular tachycardia. In spite of maintenance of ventricular rate between 90 and 110, the patient became progressively worse and expired 36 hours after admission. The clinical impression was hypertensive arteriosclerotic heart disease. A postmortem examination was not made.

Summary of Case.—Paroxysmal ventricular tachycardia was suppressed by the intravenous administration of 400 mg. of procaine amide hydrochloride. After the suppression of the ventricular ectopic focus, auricular flutter with varying A-V conduction was found.

CASE 6.—A 48-year-old man with arteriosclerotic heart disease was found to have very frequent runs of ventricular tachycardia and ventricular ectopic beats interposed with runs of irregularly conducted beats. After suppression of the ventricular ectopic beats and paroxysms by administration of 300 mg. of procaine amide hydrochloride, an auricular flutter was obvious. It was assumed that the auricular flutter and paroxysmal ventricular tachycardia were simultaneously present. The auricular flutter was subsequently converted to sinus rhythm by administration of quinidine, and the patient was discharged from the hospital after four days. Because the electrocardiograms in this and the following case contribute no additional information, they have not been presented.

CASE 7.—This patient was a 56-year-old woman with auricular flutter associated with rheumatic heart disease, in whom two short runs of ventricular tachycardia developed during cardiac catheterization. The auricular flutter was of the same rate previous to, during, and following the ventricular paroxysms. No further complications arose, and the patient was discharged to the cardiac clinic several days later.

SUMMARY AND CONCLUSIONS

Evidence of the occurrence of simultaneous dissociated tachycardias in seven patients is presented. In three the diagnosis was unequivocal, having been demonstrated electrocardiographically by conversion of paroxysmal auricular tachycardias to sinus rhythm without effect on the ventricular mechanisms. In the other four the diagnosis was inferential, auricular flutter having been present immediately after, and presumably during, runs of ventricular tachycardia. Unequivocal demonstration of the ventricular origin of the paroxysms of presumed ventricular tachycardia was not possible in the presence of faster auricular flutter rates, because aberrant ventricular conduction of transmitted auricular impulses could not be definitely excluded. In these cases the diagnosis of paroxysmal ventricular tachycardia was based mainly on the gradual widening of the QRS complexes and the gradual slowing, then suppression, of the paroxysms after intravenous administration of procaine amide hydrochloride. These were the same changes that occurred after administration of procaine amide hydrochloride in other cases of paroxysmal ventricular tachycardia.

Double tachycardias occurred in one patient receiving maintenance doses of quinidine, in two patients receiving large initial therapeutic doses of digitalis preparations, in two patients receiving maintenance doses of digitalis, in one patient receiving no cardiac drugs, and in one patient during cardiac catheterization. In the last patient auricular flutter was associated with rheumatic heart disease.

and paroxysmal ventricular tachycardia was clearly related to intracardiac contact by the catheter. In the other six patients the occurrence of paroxysmal tachycardias could not be related to drugs. Intravenously administered procaine amide hydrochloride suppressed paroxysmal ventricular pacemakers in every instance that it was used.

Exclusive of the one patient with rheumatic heart disease, on whom cardiac catheterization was performed, all these patients, whose ages ranged from 48 to 80, had definite evidence of advanced coronary disease with a history of cardiac decompensation prior to the onset of the arrhythmias described. One had a known myocardial infarction previously, and another was diagnosed clinically as having acute coronary occlusion. The patients in cases 2, 3, 4, and 5 died within 72 hours after recognition of the double tachycardias. The patient in case 1 was discharged but died during a subsequent hospitalization five months later; and the patient in case 6 was discharged and followed up in the cardiac clinic, with no recurrences of tachycardia or heart failure.

It is believed that double tachycardias occur in the course of coronary artery disease and that they indicate a severe degree of heart disease. The high mortality rate further indicates the severity of the heart disease in these patients. As does any rapid heart action, that occurring in cases of double tachycardia impairs cardiac efficiency, which, when superimposed on severe heart disease, may cause death. The recognition of two independent paroxysmal tachycardias is important in deciding what therapy is appropriate to slow the heart and relieve the burden imposed by a rapid ventricular rate in such severely ill patients. The final outcome seems to be determined primarily by the severity of the underlying heart disease.

1853 W. Polk St. (Dr. Bernstein).

CLINICAL USE OF EXTRACORPOREAL OXYGENATION WITH OXYGENATOR-PUMP

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and
Thomas L. Largen, M.D., Cincinnati

Oxygenation of the blood, elimination of carbon dioxide, and maintenance of circulation by means of a pump that has the effect of ventricular contractions constitute the objectives in mechanical substitution for the lungs and heart. A review of the physiological details involved in the development of substitutes for the lungs and the heart is beyond the scope of this report and will therefore not be attempted. Furthermore, the contributions of Kolff, Jongbloed, Bjork, Gibbon, and Dennis have already furnished answers to many of the basic problems involved in extracorporeal oxygenation and circulation.

Recent reports of work done in this field seem to have led many practitioners to believe that the use of a mechanical heart-lung machine for total by-pass during intracardiac surgery is an imminent possibility. However, the logical steps in the evolution of such physiological-mechanical systems must still include experiments designed to measure the machine's effects when used on human patients. Moreover, this evolutionary development should include studies of the effects of these mechanical devices on cardiovascular, pulmonary, and renal function during partial extracorporeal circulation as observed on vein-to-machine-to-vein and vein-to-machine-to-artery circuits in selected patients. Information derived from such controlled studies may lead to attainment of the final objective, i. e., the total extracorporeal circulation (complete by-pass of the heart and lungs), which is necessary for deliberate intracardiac surgery in a relatively bloodless field.

The following is a report of the first clinical trial of the oxygenator-pump with which the authors had been working.[1] It is believed that planned studies of this type and observations such as those reported by Dogliotti [2] may prepare a background of experience from which the procedure of total by-pass may be undertaken with reasonable safety. The fundamental problem of the patient selected was cor pulmonale and reduction of respiratory membrane surface area. The use of the apparatus in a vein-to-machine-to-vein extracorporeal circuit was therefore conceived for the purpose of studying its effect in oxygenation and elimination of carbon dioxide. Also observed were other effects on blood flowing through such an extracorporeal circuit for 75 minutes.

The patient was a 45-year-old ex-fireman whose major complaints were breathlessness and coughing of four years' duration. He had been in the Cincinnati General Hospital on five occasions between 1942 and 1951 for the following conditions: in 1942, for fever of unknown cause; in 1944, for spina bifida occulta; in 1949, for rheumatoid arthritis; in 1950, for disseminated bursitis; and in 1951, for chronic cor pulmonale, secondary to a widespread fibrotic lung lesion. In 1944 diffuse mottled lesions in both lung fields were detected by roentgenography, and in 1951 a lung

This study was supported in part by grants from the American Heart Association, the United States Public Health Service, and the Lucie Rawson Scientific Fund.

From the Department of Surgery and the Department of Pediatrics, College of Medicine of the University of Cincinnati, and from the Fels Institute for Research in Human Development, Antioch College, Yellow Springs, Ohio. Dr. Clark is chairman of the Department of Biochemistry of the Fels Institute for Research in Human Development.

Dr. Louis G. Herrmann provided laboratory facilities and other assistance, and Miss Molly MacKenzie and Miss Ruth Parker gave technical assistance in this study. Miss Mary Alice Costello, Director of the Department of Anesthesia of the Cincinnati General Hospital, and Mrs. Mary Gustafson, student anesthetist, aided in the management of the patient. Dr. K. W. Thompson of Organon Inc., Orange, N. J., provided materials and technical advice for this study.

1. Helmsworth, J. A., and others: Artificial Oxygenation and Circulation During Complete By-Pass of the Heart, J. Thoracic Surg., to be published.

2. Dogliotti, A. M.: Clinical Use of the Artificial Circulation with a Note on Intra-Arterial Transfusion, Bull. Johns Hopkins Hosp. 90: 131-133, 1952.

biopsy showed diffuse interstitial fibrosis of nonspecific nature.[3] This lesion was not characteristic of silicosis, and spectrographic assays of the lung biopsy for beryllium were negative. During the seven months before his last admission, the patient's respiratory symptoms had progressed until he was dyspneic, orthopneic, and cyanotic at rest. For two weeks prior to the study, his dyspnea and cyanosis were so severe that even the effort of conversing produced breathlessness. His cough was productive of about 1 oz. (28.4 gm.) of mucopurulent, blood-free sputum per day. During the preceding five months he had been in congestive heart failure, as evidenced by increased jugular venous pressure, the presence of rales at both lung bases, hepatomegaly, and pitting edema of legs and feet. Moderate cardiac enlargement was present, and a grade 2 systolic murmur, with splitting of the second heart sound, was audible over the pulmonary area.

In addition to the diffuse lesions in both lung fields, the chest roentgenogram showed prominence of the pulmonary artery and enlargement of the right ventricle (fig. 1). Electrocardiographic evidence of right ventricular hypertrophy was present. Cardiac catheterization performed seven months earlier showed a pressure

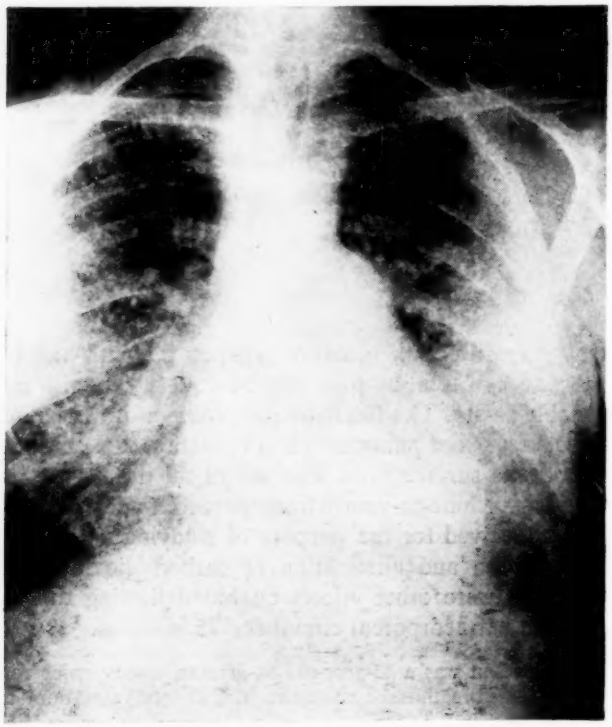


Fig. 1.—Roentgenogram of patient prior to experiment of mechanical oxygenation, showing, in addition to diffuse lesions in both lung fields, prominence of pulmonary artery and enlargement of right ventricle

of 70/26 mm. Hg in the pulmonary artery, a pulmonary capillary pressure of 8 mm. Hg, and a mean right auricular pressure of 10 mm. Hg. The cardiac index was 2.9 liters per minute per square meter of body surface, and the pulmonary arteriolar resistance was 466 dynes second cm^{-5}. The patient had been digitalized and was maintained on 0.2 mg. of digitoxin daily, was given 2 cc. of meralluride (mercuhydrin®) sodium solution intramuscularly on alternate days, and was kept on a low sodium chloride diet.

The oxygenator-pump was sterilized by autoclaving. Four liters of sterile isotonic sodium chloride solution containing 10 cc. of 5% triton® (a nontoxic, nonhemolytic detergent) were circulated through the machine for 10 minutes, and an additional 12 liters of sterile sodium chloride solution were used for a final rinsing.[1] The apparatus was then filled with 1,500 cc. of blood that, in addition to the usual cross matching, had been treated by the adding of 60 mg. of heparin sodium (Organon) and 1 gm. of calcium gluconate.

3. Katz, H. L., and Auerbach, O.: Diffuse Interstitial Fibrosis of the Lungs (Report of Case with Unusual Features), Dis. Chest **20**: 366-377, 1951.

On April 3, 1952, the patient was premedicated with ½ grain (0.03 gm.) of codeine, which was later supplemented by 1 grain (0.06 gm.) of codeine. The skin over both inguinal areas and the right antecubital fossa was prepared in the standard manner. Next, both saphenous veins, after being exposed close to their junction with the femoral vein under infiltration anesthesia, were

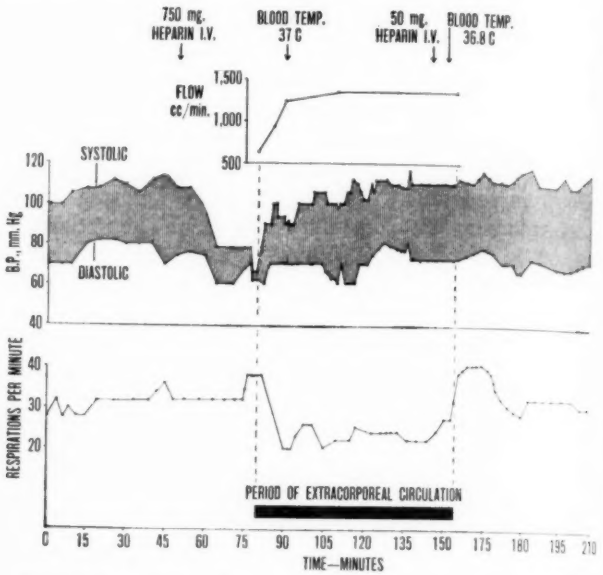
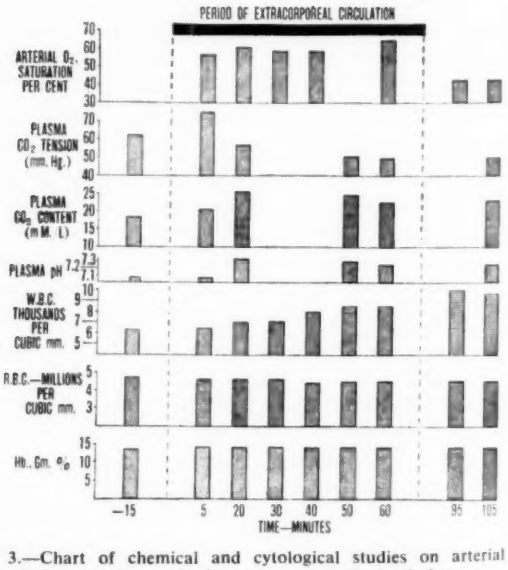


Fig. 2.—Chart of blood volume flow through extracorporeal circuit, showing blood pressure and respiratory rate before, during, and after extracorporeal circulation.

catheterized with long, fenestrated koroseal® tubes, the tips of which were advanced into the inferior vena cava, close to the right auricle. Through these catheters, unsaturated venous blood was withdrawn for oxygenation in the extracorporeal circuit. Two veins in the right antecubital fossa were exposed and cannulated with short polyethylene tubes. These cannulas served as avenues for the return of oxygenated blood from the machine to


PERIOD OF EXTRACORPOREAL CIRCULATION
ARTERIAL O_2 SATURATION PER CENT
70 60 50 40 30
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PLASMA CO_2 CONTENT (m M. L)
25 20 15 10
PLASMA pH 7.2 7.3 7.1
W.B.C. THOUSANDS PER CUBIC mm.
10 9 8 7 6 5
R.B.C.—MILLIONS PER CUBIC mm.
5 4 3
Hb. Gm. %
15 10 5
−15 5 20 30 40 50 60 95 105
TIME—MINUTES

Fig. 3.—Chart of chemical and cytological studies on arterial blood samples before, during, and after extracorporeal circulation.

the superior vena cava. All samples of arterial blood were collected by means of an indwelling needle placed in the right brachial artery. The patient's blood was rendered incoagulable by the intravenous injection of 750 mg. of heparin sodium (10 mg. per kilogram of body weight). Soon after the heparin was infused, it was noted that the blood pressure fell and that the respiratory rate rose. These changes, as well as a period of shivering, lasted while final connections were made between the apparatus and

the tubes for withdrawing blood from the patient and returning it to him from the machine.

Observations During and After Extracorporeal Circulation.—The flow through the apparatus was made to increase from 640 cc. per minute to 1,280 cc. per minute over a period of 10 minutes. (This is by no means the maximum performance of the apparatus. In dogs weighing 15 kg., a flow of 2.5 liters per minute is not unusual.) At the time this flow rate was obtained and during its subsequent increase to 1,360 cc. per minute, subjective and objective signs of the patient's improvement were manifest (fig. 2). He volunteered the fact that his dyspnea was relieved and that he could lie on his back without discomfort. His apprehension, not adequately controlled before pumping, was relieved during this period of extracorporeal circulation, and he remained asleep throughout most of the 75 minutes of partial extracorporeal circulation. The respiratory rate had a prepumping level of 32 to 38 per minute; it fell to 20 to 26 per minute during extracorporeal oxygenation. Concomitant with the relief of dyspnea, there was a striking diminution in the degree of cyanosis. The pulse rate remained between 80 and 90 per minute during the whole procedure, except for a tachycardia of 130 per minute, which lasted for 15 minutes prior to pumping. Electrocardiographic tracings showed no arrhythmias. Within 10 minutes after completion of the period of extracorporeal circulation, there was a reversal of all the above signs to the patient's original state of cardiorespiratory dysfunction.

The control sample for arterial oxygen saturation was not suitable for analysis. During the period of partial by-pass of the heart and lungs, the arterial oxygen saturation varied from 58 to 65% (fig. 3). Oximeter readings, taken with a Kramer photoelectric cell and a millivoltmeter, indicated that the oxygen saturation of the blood flowing from the oxygenator-pump back into the patient was never less than 90%. As pointed out above, only part of the venous return to the heart was withdrawn for circulation through the oxygenator, this portion amounting to an estimated one-fourth to one-third of the cardiac output. It is therefore not surprising that the arterial oxygen saturation did not rise to higher levels. Samples taken from the brachial artery after the completion of the period of extracorporeal oxygenation showed a prompt fall in the oxygen saturation to 43%.

Because the blood is exposed to some effects of turbulence as well as suction and pressure during its passage through the apparatus, hemograms and plasma hemoglobin determinations were made before, during, and after pumping. It will be noted in figure 3 that the hemoglobin content and the red blood cell count did not vary. The total white blood cell count rose from a prepumping level of 6,400 per cubic millimeter to from 7,000 to 10,000 per cubic millimeter during oxygenation. This count was 9,900 per cubic millimeter 40 minutes after completion of pumping and was 12,300 per cubic millimeter 24 hours later. The differential white blood cell count in the control period was as follows: polymorphonuclear neutrophils, 87%; lymphocytes, 10%; and eosinophils, 3%. There was no significant shift in the distribution of cells during the pumping period; and 40 minutes after the by-pass the differential count showed the following: polymorphonuclear neutrophils, 88%; lymphocytes, 10%; and eosinophils, 2%. There was no evidence of hemolysis on inspection of the supernatant plasma of the specimens of blood obtained during and after pumping. Spectroscopically, each plasma specimen showed a faint band of absorption at 570 mμ, but the quantity of hemoglobin was too small to be determined accurately by routine methods.

The preliminary blood specimen taken before the period of extracorporeal circulation showed that there was marked respiratory acidosis, with the plasma pCO_2 at 62 mm. Hg and the plasma pH 7.06 (fig. 3). The preliminary value for total plasma bicarbonate content of 18.3 mM. per liter indicated lack of renal compensation, which should have produced elevation of the plasma bicarbonate. When extracorporeal oxygenation was begun, plasma carbon dioxide tension rose and then fell gradually to around 50 mm. Hg. Plasma pH rose during oxygenation. These changes occurred in association with elevation of total plasma bicarbonate. It is evident, then, that during oxygenation, values for plasma pH, pCO_2, and total bicarbonate showed distinct improvement. Determinations of the serum protein, chloride, and carbon dioxide levels, the blood urea nitrogen level, and the prothrombin time were made 12 hours before and 12 hours after the period of extracorporeal circulation. There was no significant variation between the values obtained for these two series. Urinalysis was repeated frequently throughout the patient's hospital stay, and there was no microscopic hematuria or other abnormality. A culture of the blood from the apparatus was sterile.

Four hours after completion of the extracorporeal circulation, blood from the antecubital and right inguinal incisions failed to clot. Protamine sulfate, 100 mg. in 200 cc. of 5% glucose in water, was slowly given intravenously. This was followed by the slow infusion of 500 cc. of whole blood. These two measures served to return the clotting time to normal. There was no evidence of postoperative jaundice, hemoglobinuria, or pulmonary embolization. The only further treatment that the patient received for the remainder of his hospital stay was chloramphenicol, maintenance doses of digitoxin and meralluride sodium solution, and a low sodium chloride diet. He was discharged from the hospital 10 days after the study in the same state of cardiorespiratory dysfunction as prior to his admission.

After 10 days at home, it was necessary for the patient to reenter the hospital. Dyspnea and orthopnea had become severer, and there was a superficial infection of the incision site in the left thigh. He died on the fourth hospital day, and a complete necropsy was performed. The gross pathological diagnosis was chronic interstitial pneumonitis and cor pulmonale. There were fresh emboli in the right heart and lung, and it was believed that these masses had come from a thrombophlebitic process in the right thigh and lower abdominal wall on the same side.

SUMMARY

Extracorporeal oxygenation and circulation were successfully performed in a specially selected patient for a period of 75 minutes. Striking relief of cyanosis, dyspnea, and orthopnea occurred during the period of dispersion-oxygenation. The plasma pH, pCO_2, and total bicarbonate were distinctly improved by the circulation through the oxygenator-pump. The leukocytes, platelets, erythrocytes, serum protein, and prothrombin time were not significantly altered by being circulated through the extracorporeal unit. This trial of a heart-lung apparatus was apparently without harmful effect on the patient.

The Broad Street Pump.—The story of the Broad Street pump in Soho from which 500 deaths from cholera resulted in August, 1854, . . . is perhaps the most famous of all epidemiological investigations, and in the history of bacteriology Snow's report on this epidemic of water-borne cholera played an important part both in establishing the doctrine of specificity of infectious disease and in indicating that fecal pollution of drinking water was the major cause of intestinal disease. Cholera had been prevalent to some extent in London since 1848, and cases had been occurring in the Soho district in small numbers during August, 1854. Then on the afternoon of August 30 an explosive and intensely lethal outbreak of cholera began. Next day there were 31 deaths and on the days following 131, 125, 58, 52 and 26. There was of course panic, a disorganized exodus from the district and overcrowding of the hospitals. Florence Nightingale served as a volunteer nurse at the Middlesex Hospital. . . . The investigations of John Snow clearly incriminated the water from what was called the Broad Street pump, and . . . the distribution of those who were infected and those who escaped in the first explosive phase of the epidemic was almost strictly correlated with whether they had or had not used the well water. The picture is very similar to that of any water or milk-borne epidemic. There were the usual dramatic contrasts. A factory in Broad Street had 22 deaths but a brewery also in Broad Street escaped, presumably because the workers had no interest in drinking water.—Sir Macfarlane Burnet, The Seeds of Time: The Impact of Microbiology on Human Affairs Since Lister's Day, *Medical Journal of Australia*, June 14, 1952.

WHITE BLOOD CELL CHANGES IN CLINICAL DISORDERS

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It is the purpose of this presentation to call attention to some of the significant changes that occur in the white blood cells in certain clinical disorders. The variations under consideration are numerical, morphological, and histochemical. It should be clearly understood that we feel the general clinical picture is much more important in diseased conditions than variations that may occur in the white blood cells. These changes constitute only one component of the total data. We have been concerned, at times, with the tremendous emphasis given to white blood cells in the interpretation and diagnosis of pathological states. While it is true that variations may be found in the white blood cell picture in many clinical disorders, it is equally true that knowledge of the white blood cell findings is not necessary in order to establish a diagnosis in the majority of them.

Further, erroneous diagnoses may result from placing too much reliance on the white blood cell picture. In this connection, it can be mentioned that one of us had the unique opportunity of seeing how far certain white blood cell findings alone would carry one in regard to the clinical diagnosis in cases of tuberculosis some years ago. It was his privilege to select patients with known clinical diagnoses for blood examinations by persons highly trained in the technique of detailed white blood cell studies. It was found that these studies led to the correct evaluation of the majority of the patients, but there were many exceptions; further, it was most unusual for the white blood cell studies to uncover something that was not already known in regard to the patient's condition. So many conditions result in minor changes in the white blood cell picture that it is necessary in the case of any clinical disorder, such as tuberculosis, for one to be sure that every other disorder is eliminated before making a statement as to presence or absence of a particular stage of development. Tuberculosis has been mentioned because so much was written 15 to 20 years ago on this subject. The situation has become stabilized now, the white blood cell picture being taken as only one small part of the clinical picture in tuberculosis. Much the same could be said about other clinical disturbances. It is accepted by everyone that neutrophilic leukocytosis with a shift to the left, eosinopenia, and lymphopenia point to infection, but it is well recognized that other conditions may produce the same picture. No well-trained surgeon would operate for appendicitis purely on the basis of the white blood cell picture. Further, reappearance of eosinophils, disappearance of a shift to the left and of neutrophilic leukocytosis, and the appearance of monocytosis, other things being equal, indicate the recovery phase of an illness, but what good clinician has to wait for these data in order to tell that a patient is improving?

The total number of white blood cells in the peripheral blood may be of help clinically, but in most instances this is of no great clinical importance. It is well recognized that leukocytosis may occur in most bacterial infections, marked tissue destruction, acute hemorrhage, acute hemolysis, certain metabolic disturbances, metastases to the bone marrow, physical exertion, and the newborn. On the other hand, exceptions are known to occur not uncommonly. Further, leukopenia may occur in certain acute infectious diseases, particularly those of viral origin and those due to typhoid-paratyphoid group of organisms; intrinsic medullary disease; hypersplenism; nutritional deficiency; intoxication with some chemical and physical agents; and anaphylaxis. The clinician, however, does not make the diagnosis solely on the basis of leukopenia; indeed, leukopenia contributes only a small amount to the diagnosis in such instances. However, in certain patients the level of the white blood cell count is of major importance. This is true, in particular, in patients being treated by irradiation and in those receiving certain drugs, such as aminopyrine, barbiturates, benzene, bismuth arsphenamine sulfonate, chloramphenicol, aminodimethylpyrazolon-quinoline-sulfonate, cinchophen, dinitrophenol, gold salts, methimazole, neocinchophen, nitrogen mustard, organic arsenic compounds, pyrithyldione, procaine amide hydrochloride, quinine, sulfonamides, thiouracil, trimethadione, and tripelennamine hydrochloride. Patients receiving irradiation or drugs such as these should be watched closely in regard to the level of the white blood cells and the total number of granulocytes. Any appreciable decrease in of the level of the white blood cells in such patients should be taken as a distinct warning.

EFFECT OF CHLORAMPHENICOL

Special attention is called to chloramphenicol, since this substance is so widely used and since there seems to be no clear understanding generally that this is a drug that can produce agranulocytosis and even aplasia of the bone marrow in certain instances. Attention was first called to this in a report by Volini and co-workers [1] in 1950. The following report of a case illustrates such a probable reaction to chloramphenicol therapy.

CASE 1.—O. C., a 28-year-old white man, was admitted to Wadsworth General Hospital in January, 1952, because of weakness, dizziness, increasing fatigue, and pallor. He had had severe bronchial asthma since 1946, with repeated attacks precipitated by frequent febrile respiratory infections. Attacks of asthma occurred during the year prior to admission at intervals of about 10 to 14 days. The attacks had seemed to be alleviated by chloramphenicol therapy, and, as a result, the patient estimated that he had received this antibiotic for about 2 out of each

Read before the General Scientific Meetings at the 101st Annual Session of the American Medical Association, Chicago, June 13, 1952.

The bibliographic references have been omitted because of lack of space; however, they will appear in the authors' reprints.

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Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions of the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

10 days for a year prior to admission (usual dosage, 2 to 3 gm. per day). In addition to the above-mentioned symptoms, which began shortly before admission, there was a history of a recent tendency to bruise severely from minimal trauma. Aside from occasional medication with aminophylline, ephedrine, and epinephrine, there was no history of exposure to other chemical agents.

Physical Examination.—At the time of admission the patient was pale; a grade 2 systolic murmur was heard widely over the precordium, and there were large ecchymotic areas on the right leg associated with moderate edema and subsiding thrombophlebitis of the extremity. The thrombophlebitis had followed a mild injury of the right leg sustained one week prior to admission. The initial hemogram showed red blood cells 2.5 million per cubic millimeter, hemoglobin, 7.6 gm. per 100 cc, packed cell volume 20%, reticulocytes 2.7%, and white blood cells 3,500 per cubic millimeter, with 11% stab forms, 21% segments, 66% lymphocytes, and 2% monocytes. The platelets were markedly decreased on the blood smear; the bleeding time (Duke) was 10 minutes; the coagulation time was 7 minutes; and there was no clot retraction in 24 hours. The result of the Coomb's test was negative. The prothrombin concentration was 100% of normal. A urinalysis, an electrocardiogram, and a roentgenogram of the chest revealed normal findings. The Wassermann reaction was negative. The stools were negative for occult bood on two occasions and faintly positive on a third determination. Aspiration of sternal bone marrow revealed a paucity of all cellular elements and a markedly hypoplastic marrow.

It was felt that the patient had hypoplastic anemia probably secondary to chloramphenicol therapy. The patient during his hospitalization had several attacks of asthma, relieved by treatment with aminophylline, potassium iodide, and hydration. During the month he was in the hospital he required 3,500 cc. of whole blood by transfusion to maintain his erythrocyte count in the neighborhood of 3,500,000 per cubic millimeter. The platelets remained decreased. Mild bleeding of the gums was the only clinical evidence of a bleeding diathesis during this time. The leukocyte count and polymorphonuclear neutrophil percentage remained about the same as on admission. His hemogram began to improve in March, 1952. He required no further transfusions, and the red blood cells returned to essentially normal values. The platelets increased in number, and the ease of bruising disappeared. At the time of writing, the leukocyte count had risen to almost 5,000 per cubic millimeter and the neutrophil percentage had likewise increased. The patient appeared to be recovering from hypoplastic anemia presumably induced by prolonged intermittent treatment with chloramphenicol. The estimated total dose of this agent received during the previous year was in excess of 100 gm. Figure 1 shows the pertinent hematological data in this case.

Comment.—The data in this case strongly support the suspicion that chloramphenicol therapy was responsible for the marked derangement in the hematopoietic functions. However, it cannot be stated unreservedly that chloramphenicol was the responsible agent.

EFFECT OF IRRADIATION

Leukopenia secondary to irradiation has been recognized for many years. Indeed, reduction of the number of circulating white blood cells is one of the oldest methods for detection of irradiation effects. A complete explanation for the production of leukopenia by roentgen rays is not at hand, but an understanding of the mechanism involved has been advanced tremendously by recent work in various sections of this country. An excellent review of this field may be found in a paper by Dowdy and Bennett.[2] The toxic effects of treatment with roentgen rays, of which leukopenia is an important one, have been shown to be reduced appreciably by (1) preirradiation medication with cysteine [3] or glutathione [4]; (2) maintenance of low temperatures during and after irradiation, which has been applied only in tadpoles and frogs and has given only temporary protection [5]; (3) irradiation of animals under anoxic conditions (5% oxygen and 95% nitrogen atmosphere) [6]; (4) splenic shielding at the time of irradiation or transplantation of part of a nonirradiated spleen into the peritoneal cavity of a previously irradiated animal [7]; (5) intravenous or intraperitoneal injections of bone marrow suspensions after irradiation [8]; (6) massive post-irradiation cross transfusions [9] and parabiosis [10]; (7) replacement transfusions of blood immediately after irradiation [11]; this result has been questioned by Allen and co-workers [12]; (8) treatment with aureomycin or combined aureomycin and streptomycin after irradiation.[13]

Further, some experiments have demonstrated means of increasing the effects of irradiation. Thus, thyroxin-medicated rats have been shown to have an increased rate of mortality when compared with the controls.[14] Also, stress has been shown to accelerate and increase the mortality of rats after irradiation.[15]

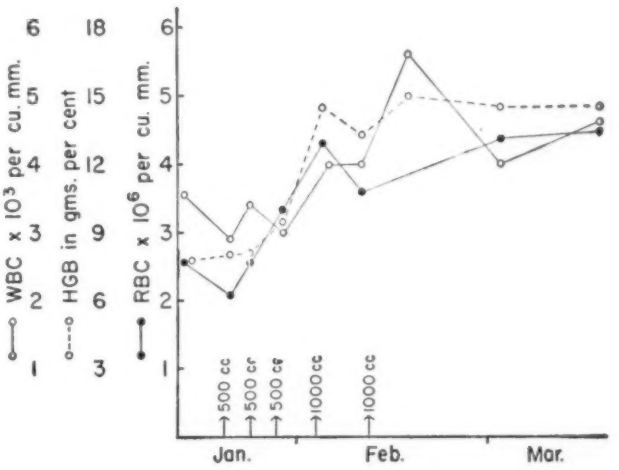

Fig. 1.—Principal hematological data in case 1 (O.C).

The lymphocyte is the most radiosensitive of all the white blood cells, 5 to 25 r to the whole body being sufficient to produce a reduction in these cells whereas 50 to 100 r is required to cause a temporary increase followed by a reduction in granulocytes.[16] As a practical procedure, the most important change in the white blood cell picture of a human being exposed to irradiation is a reduction in the total number of the cells, which is due predominantly to depreciation in the number of granulocytes since these represent the majority of the cells in the blood of the average human being.

No discussion of leukopenia due to irradiation would be complete without some reference to possible increased sensitivity to irradiation of the white blood cells in patients with leukemia as compared with nonleukemic subjects. In leukemic subjects, relatively small amounts of irradiation (400 to 700 r in fractional doses of as little as 25 to 50 r) over the chest and/or spleen may produce precipitous drops in the number of circulating white blood cells. A similar effect may be produced in nonleukemic subjects with generally much larger amounts

of irradiation. However, in the treatment of Hodgkin's disease or lymphosarcoma, similar amounts of radiation to corresponding areas not infrequently result in a marked reduction in the number of circulating white blood cells. No satisfactory explanation has been offered for this possible increased sensitivity in the white blood cell response. There is no compelling reason for one to assume that the circulating cells in leukemia are peculiarly sensitive to radiation in contrast with the normal. Even if this were the case, it would not explain the persistence of the leukopenia following irradiation, since destruction in the peripheral blood would soon be corrected by active bone marrow.

One can postulate that in cases of leukemia there are abnormal chemical, cellular, and tissue changes that may be such as to yield, as a result of exposure to irradiation, a product or products that interfere with the manufacture of white blood cells, or, alternatively, that the metabolism of leukemic tissues is such as to render them more sensitive to the normal effects of irradiation. No proof of such conditions exist, but the possibility cannot be excluded, and the clinical fact must be borne in mind forcibly when one is treating patients with leukemia, since leukopenia, with its added liabilities, can be readily produced by irradiation of leukemic subjects in too large amounts.

Another point worthy of consideration relates to the fact that leukopenia is said to be produced at times by irradiation over relatively small areas of active hematopoietic tissue in subjects with normal hematopoietic systems. This raises the question of an effect being produced on blood-forming tissues outside the areas directly irradiated. On purely clinical grounds, the evidence is strongly in favor of such an indirect effect of irradiation. Thus, leukopenia develops on occasions when irradiation is limited to the pelvic area or some other localized region. Many investigators have attacked this problem in a variety of ways, e. g., presence or absence of toxins and/or chemicals or enzymes and morphological changes in hematopoietic tissues not in the irradiated fields. A detailed survey of the literature relating to this subject was made in an article by Lawrence, Valentine, and Dowdy [16] in 1947, at which time an attempt was made to find an explanation to the problem by the use of cross circulation experiments in cats. At that time, the authors were forced to the conclusion that no indirect effects peculiar to radiation could be detected by means of changes in the white blood cell picture under the conditions of their experiments. In these experiments, the attempt was made to detect some change in the white blood cell picture of a nonirradiated cat as a result of cross circulation with an irradiated cat. In other words, evidence for production of some leukopenia-producing substance in the irradiated area and the later transmission of this to another animal by cross circulation was sought. Since it is now known that shielding of the spleen and/or other areas offers great protection against irradiation,[7] it may be that toxic substances produced by irradiation in the one animal were neutralized by humoral or other factors in the nonirradiated animal so as to prevent any detection of them in the latter animal. Tremendous doses of irradiation were used, thus precluding the detection of some favorable action in the treated animal by humoral or cellular substances from the normal animal. Among other factors that deserve consideration in this connection are the general physical status of the patient, nutritional disturbances secondary to the effects of radiation to the gastrointestinal tract, the bacterial flora of the gastrointestinal tract, general radiation sickness, and the amount and degree of total body irradiation resulting from scattered irradiation.

In connection with the subject of irradiation and its effect on the hematopoietic tissues, we have encountered a group of cases that have definite clinical interest. It has been known for a long time that splenectomy is beneficial in cases of congenital hemolytic anemia, idiopathic thrombocytopenic purpura, and certain diseases associated with hypersplenism. Nonetheless, it has been only recently that splenectomy has been shown to be of benefit in some patients with lymphomatous disease plus hypersplenism who have undergone prolonged x-ray treatment. It is interesting to note that Bennett [17] demonstrated that certain features of the hypersplenic picture could be produced in normal rats subjected to prolonged irradiation. Accordingly, in a few selected patients, we have tried the effect of splenectomy as indicated in the following two cases.

CASE 2.—R. L. Mc., a 22-year-old white male Navy veteran, first noted bilateral swelling of the neck, without other symptoms, in November, 1949. He was admitted to a naval hospital in May, 1950, where multiple lymph node biopsies were done and a diagnosis of Hodgkin's disease was established. He was treated with roentgen rays, 2,000 r * to the lymph-bearing areas, and obtained a good response. In February, 1951, there was recurrence of fever, weakness, and cervical adenopathy. Biopsies of cervical masses demonstrated, in addition to Hodgkin's disease, a typical picture of tuberculous lymphadenitis. Treatment again consisted of the administration of 2,000 r, after which there was a decided fall in the white blood cell count. Then, a three month's course of treatment with streptomycin and para-aminosalicylic acid was given.

There were several minor episodes requiring hospitalization during the remainder of 1951. The patient was observed for tuberculosis of the kidneys, but this was shown not to be present. Several severe respiratory infections developed, one having been diagnosed as viral pneumonia. Whole blood transfusions were given because of progressive anemia. No further treatment was given after June, 1951.

In November, 1951, the patient was admitted to the Wadsworth General Hospital because of a respiratory infection that had not responded to penicillin therapy. In addition, furunculosis of the skin, associated with pronounced leukopenia (500 white blood cells per cubic millimeter) had developed. The past and family histories were noncontributory.

Physical Examination (Admission).—The patient's height was 5 ft. 9½ in. (177 cm.) and his weight 160 lb. (72.6 kg.). His temperature was 99 F, pulse rate 106, and blood pressure 105/55. He was well developed and nourished but appeared chronically ill, and had moderate pallor. There were firm, matted, nontender groups of nodes in both cervical regions, measuring 3 by 6 cm. on the right and 4 by 9 cm. on the left. The skin was erythematous on the right; there were four linear healed scars above the clavicles. Small, shotty nodes were observed in the cervical chains, both axillas, and inguinal groups; in the inguinal areas the nodes were probably larger than nor-

* The exact amounts given to each of the several areas covered by roentgen-rays is unknown, since the patient was treated at several different hospitals.

mally expected. The heart and lungs were normal. Examination of the abdomen revealed the spleen to be palpable 4 cm. below the left costal margin and the liver 2 cm. below the right costal margin. No masses were felt. A biopsy scar was present in the right inguinal region. The remainder of the examination was essentially negative.

Laboratory Data.—The white blood cell count was 550 per cubic millimeter, with 2% eosinophils, 7% stab forms, 1% segmented neutrophils, 67% lymphocytes, and 23% monocytes. The red blood cell count was 3,500,000 per cubic millimeter, hemoglobin 12 gm. per 100 cc., volume of packed red blood cells 32%, and sedimentation rate (Wintrobe) 15 mm. in one hour. The platelets were reduced on a smear of the peripheral blood. The urine was normal. A roentgenogram of the chest revealed normal findings. An aspirated specimen of sternal marrow showed mild normoblastic hyperplasia and some inhibition of maturation of the myeloid cells. The Wassermann reaction of the blood was negative.

Hospital Course.—The patient was treated with semi-bedrest and a procaine penicillin G preparation (crysticillin®), 300,000 units each day, because of respiratory symptoms. He received a total of 3,000 cc. of whole blood prior to and after operation. It was thought likely that the previous drug and radiation treatment he had received were not of sufficient quantity to cause the profound leukopenia. His highest white blood cell count, prior to surgery and at a time when he had lobar pneumonia, was 1,600 per cubic millimeter, with 26% granulocytes, the other elements remaining about constant within the above-noted figures. He was subjected to splenectomy on Dec. 31, 1951. The operative procedure was uncomplicated. The spleen, weighing 1,650 gm., was removed and, when examined with a lymph node from the splenic pedicle, revealed suggestive evidence of Hodgkin's disease and, also, scattered miliary tuberculosis with caseating necrosis. On the third postoperative day the white blood cell count was 7,500 per cubic millimeter, with 1% basophils, 69% granulocytes, 4% lymphocytes, and 26% monocytes. An occasional normoblast was noted. Subsequently, the white blood cell count leveled off at about 5,000 per cubic millimeter, with a fall again in granulocytes to about 10% to 20%. Subjectively, the patient made a good recovery; he was ambulant with no symptoms. He was given brief local roentgen therapy, 1,600 r, to recurrent enlarging nodes in the right cervical region, prior to discharge in February, 1952, five weeks after splenectomy.

CASE 3.—A. G. F., a 55-year-old white male machinist, first became ill in December, 1944, with pallor, weakness, squint, and generalized lymphadenopathy. A biopsy of tissue from the eyelids and later from an enlarged inguinal lymph node revealed findings typical of lymphocytic lymphosarcoma in April, 1945. Between April, 1945, and October, 1950, he received large amounts of irradiation, i. e., 1,000 r to each cervical area, 4,275 r over the mediastinum, 3,600 r to the epigastric area, 2,675 r to the right inguinal and 1,600 r to the left inguinal area, 1,000 r to the left axillary region, 850 r to the spleen, and 600 r to the liver. In December, 1948, after further roentgen therapy for subcutaneous masses that had reappeared over the extremities, with attendant edema, his hemogram was first noted to be abnormal. Mild anemia and leukopenia disappeared with cessation of radiation. Increasing splenomegaly associated with progressive severe anemia, requiring multiple transfusions, was observed in April, 1949. Despite cautious continued roentgen therapy (last treatment in October, 1950) his condition became poorer, with anorexia, weight loss, and recurrent tumor formation in many sites. He was admitted for the last time in January, 1951, because of fever, productive cough, and increasing dyspnea. The family and personal histories were noncontributory.

Physical Examination.—The patient's temperature was 101 F, pulse rate 94, and blood pressure 115/70. He was fairly well developed and nourished but appeared acutely ill, with coughing and slight dyspnea. The pharynx was injected. There were dullness and diminished breath sounds with crepitant rales at the left lung base. Scattered fine rales were also heard at the right lung base. A grade 2 systolic murmur was present along the left sternal border. The spleen was palpable 2 cm. below the costal margin and the liver 1 cm. At the time of original examination there were no subcutaneous masses and no lymphadenopathy.

Laboratory Data.—The red blood cell count was 3,800,000 per cubic millimeter, hemoglobin 76.0%, and white blood cell count 1,750 per cubic millimeter, with 1% eosinophils, 4% segmented neutrophils, 81% lymphocytes, and 14% monocytes. Urinalysis revealed nothing remarkable. The Wassermann reaction of the blood was negative. The bleeding and clotting times were normal. A blood culture produced no growth. A roentgenogram of the chest demonstrated an infiltration in the lower left lung field and equivocal mediastinal widening. A bone marrow specimen aspirated from the iliac crest was interpreted as showing maturation arrest of the myeloid series at the myelocyte level. There was, also, a slightly increased number of lymphocytes, some of which were abnormal in appearance.

Hospital Course.—The patient was treated for pneumonia with antibiotics. The response was poor as judged by clinical signs and repeated roentgenograms of the chest. He had a continuous spiking fever with temperatures between 101 and 102 F, and complained of increasing sore throat. White blood cell counts ranged between 850 and 1,750 cells per cubic millimeter, with neutrophils less than 10%. Progressive splenomegaly, subcutaneous infiltrations in the left forearm and thigh, and increasing size of the axillary and inguinal nodes were observed during the first two weeks of the patient's hospitalization.

The patient underwent splenectomy, with spinal anesthesia, on Jan. 25, 1951. The spleen weighed 1,300 gm. and showed lymphoid follicle hyperplasia on section. Immediately after surgery

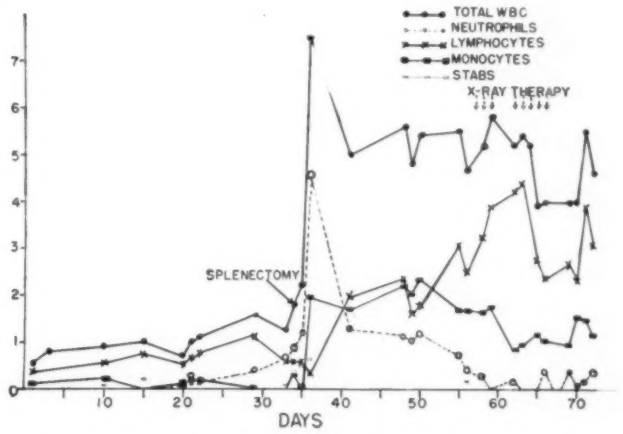

Fig. 2.—White blood cell findings in case 2 (R.L.Mc.) before and after splenectomy.

the white blood cell count rose to 8,600 per cubic millimeter, with 33% stab forms and 47% segmented neutrophils. On the seventh postoperative day a leukemoid picture was noted, with 73,500 white blood cells per cubic millimeter, and a differential count of 6% myelocytes, 2% juvenile forms, 20% stab forms, 69% segmented neutrophils, and only 1% lymphocytes. Occasional nucleated and abnormal red cells were present. The red blood cell count fell from 4,200,000 to 2,900,000 per cubic millimeter. On the eighth postoperative day, the patient, otherwise convalescing well, suddenly expectorated a small amount of bright red blood. It was thought that he probably had a small pulmonary infarction. Heparin therapy was begun with a base line clotting time of 14 minutes. Shortly afterward the patient vomited about 30 cc. of blood and went into profound shock, from which he did not recover despite intensive therapy. He died on Feb. 2, the eighth postoperative day. Autopsy disclosed massive gastrointestinal hemorrhage from an unsuspected gastric ulcer.

Comment.—These cases are thought-provoking, since they demonstrate clearly that, regardless of whether the leukopenia was due to irradiation, it was responsive to splenectomy. In other words, the leukopenias were not due to bone marrow depletion. One can ask whether the disease, an overactive spleen, or both were responsible for the low white blood cell levels.

The first patient (case 2) had had leukopenia for 10 months after his last course of x-ray therapy. He had a prompt, but not pronounced, increase in the number of white blood cells in his peripheral blood after splenectomy (fig. 2). He maintained this elevation of his white blood cell count until he was discharged, five weeks later, but his neutrophils returned to their previous low levels. Whether the slight drop in the total number of white blood cells following x-ray therapy to enlarged nodes in his right cervical area was due to irradiation cannot be stated. It does, however, raise the question as to whether radiation of this amount over a small area such as this could, in such a patient, produce an effect on the total number of white blood cells.

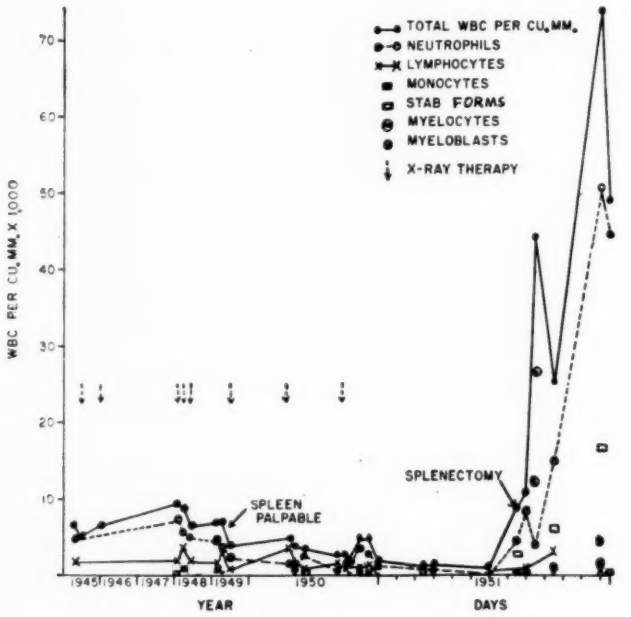

Fig. 3.—White blood cell findings in case 3 (A.G.F.) before and after splenectomy.

The second patient (case 3) had severe leukopenia that had developed in association with x-ray therapy. His last exposure to irradiation had been approximately three months prior to splenectomy. Certainly, there was strong evidence that the leukopenia was due to irradiation. In spite of this, there was a pronounced and spectacular neutrophilic leukocytosis after operation (fig. 3). It is regrettable that we were unable to follow him longer, owing to his death from gastrointestinal bleeding.

Another type of leukopenia to which we wish to call special attention at this time is the chronic idiopathic variety, about which relatively little is known. In many patients with this condition, splenomegaly constitutes part of the picture, but this is not true of all such patients. When there is splenomegaly and, to a lesser degree, even when splenomegaly cannot be demonstrated, the question of splenectomy must be considered. We know of no way in which one can be certain that splenectomy in a given subject will result in restitution of the normal white blood cell count. We do not feel that the result of an epinephrine test is a reliable indication of this. One remarkable patient of this type, who had had severe leukopenia for at least 16 years prior to splenectomy, in 1944, and who had restitution of a normal white blood cell picture after operation, was described by one of us (J. S. L.) in 1946.[18] Unfortunately, not all patients with chronic leukopenia of not clearly understood causation respond, as regards the white blood cells, so favorably to splenectomy.

SPLENECTOMY

When the surgical removal of the spleen is under consideration, one should attempt to settle the problem on the merits of the individual case at an early date. Otherwise, considerable difficulties are encountered and the clinician finds himself in the position of taking what amount to heroic measures. This is well amplified by the following case of leukopenia occurring in a patient with Felty's syndrome.

CASE 4.—C. F. C., a 52-year-old man, was admitted Sept. 8, 1949, with a history of migratory arthritis since 1945 with progressive disability. Five weeks prior to admission the patient had an attack of weakness, fatigue, and moderate dyspnea. He lost 20 lb. (9 kg.) in weight. Four weeks prior to admission he had noted a large mass in the left upper quadrant of the abdomen. There was a history of a penile lesion in 1916, and a strongly positive serologic reaction was noted in 1940. He had received a small amount of bismuth in 1940.

Physical Examination.—The patient was poorly nourished and developed. The liver was palpable three fingerbreadths below the costal margin. The spleen was palpable at the level of the umbilicus. There were classical findings of moderately advanced rheumatoid arthritis.

Laboratory Data.—The erythrocyte count was 3,000,000 per cubic millimeter. The white blood cell count was 1,000 to 2,500 per cubic millimeter. There was neutropenia, 10% to 20% of the cells being of the late myeloid series and the remainder being largely lymphocytes. The serologic reaction was positive. The total blood proteins were elevated to 8.1 gm. per 100 cc., with the globulin 5.1 gm. per 100 cc. The result of the cephalin flocculation test was 4+ and of the thymol flocculation test 2+. The sulfobromophthalein sodium test showed slight retention (3% at 45 minutes). The prothrombin time was consistently in the neighborhood of 30%. A roentgenogram of the chest showed probable pneumonia of the left lower lung field. This resolved with appearance of other densities in other areas.

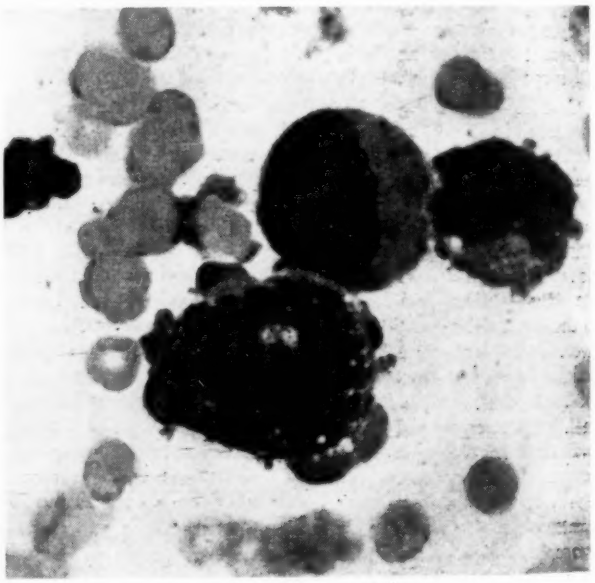

Fig. 4.—Malignant cells in bone marrow of patient with metastatic carcinoma.

Course.—The patient had repeated febrile episodes, including those associated with sore throat, recurrent pneumonitis, and multiple furunculosis. These were attributed largely to the associated neutropenia and were partially controlled by treatment with repeated courses of antibiotics. The anemia and leukopenia failed to respond to treatment with folic acid, vitamin B_{12}, or liver. A bone marrow aspiration revealed a cellular marrow with

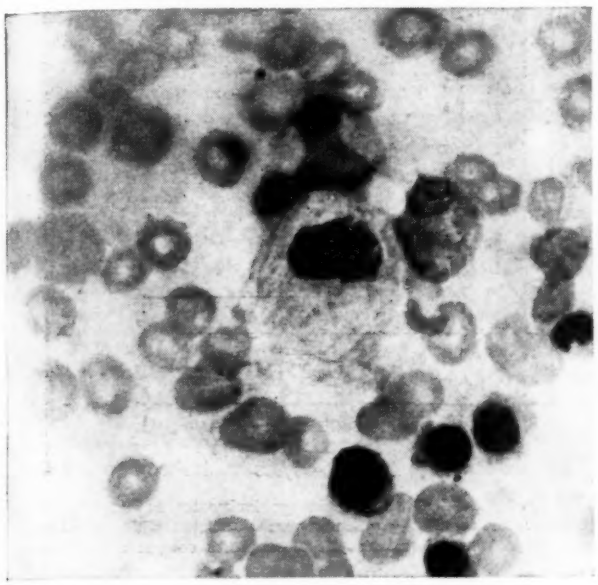

Fig. 5.—Typical Gaucher cell in bone marrow smear.

increased numbers of cells at the myelocyte level. A liver biopsy showed minute foci of necrosis and hyperplasia of the hepatic cells. From Jan. 19 to Jan. 29, 1950, the patient received a total of 400 mg. of corticotropin (ACTH). There was no change in the hematologic picture. However, urinary 11-oxysteroids failed to rise with the medication, so that he was given 900 mg. of cortisone over a nine-day period. Again, no change in the hematologic picture was observed. The patient was becoming progressively worse, and splenectomy was advised. A hemolytic reaction to transfused blood of compatible type without a positive Coomb's reaction had developed and further complicated preoperative preparation. Despite the bad risk, it was felt that splenectomy offered the only chance for survival. The patient died during surgery. The clinical impressions were Felty's syndrome, latent syphilis, and recurrent pneumonitis, with a question of pulmonary infarcts.

Comment.—It seems pertinent to state that splenectomy was postponed too long in this patient. Decision to resort to surgery should have been made before the patient's general condition had deteriorated to such a great degree. Hutt and co-workers [19] have reported beneficial effects in four patients with Felty's syndrome following splenectomy. It would seem advisable to continue doing splenectomies on patients with this syndrome until a sufficiently large number of cases has been collected to allow a final opinion to be formed.

OTHER CONDITIONS RELATED TO WHITE BLOOD CELL CHANGES

Other conditions that deserve special consideration in connection with the white blood cell picture are (1) myelophthisic anemia, on the basis of metastatic carcinoma in the bone marrow, (2) Gaucher's disease, (3) lupus erythematosus, and (4) lymphosarcoma.

Figure 4 illustrates the typical bone marrow findings in a case of metastatic carcinoma of the bone marrow. In such cases, the peripheral blood may reflect what is termed an irritative bone marrow picture, i. e., slight to moderate leukocytosis with a fairly pronounced shift to the left, increased numbers of polychromatophilic red blood cells, reticulocytosis, and normal or diminished numbers of platelets. In rare instances, the diagnosis has been suspected on the basis of the blood findings, later confirmed by section and aspiration of the marrow. It should be stated that even extensive metastases to the bone marrow may not be apparent in aspiration material obtained from a very small portion of the bone marrow.

Gaucher's disease (lipid histiocytosis of kerosin type) is mentioned because of its rarity and the lack of familiarity with the cells typical of it. This disorder is usually associated with leukopenia. Typical Gaucher cells may be found in aspiration or biopsy material from the bone marrow, the enlarged spleen, and the liver. Figure 5 depicts a typical Gaucher cell.

Lupus erythematosus is mentioned since it has only recently been shown that pathognomonic cells can be demonstrated in the bone marrow and blood of patients with this condition.[20] Figure 6 shows these cells.

Figure 7 shows typical lymphosarcoma cells, the main characteristic of which is that the nucleus appears folded upon itself. Sternberg,[21] in 1905, first called attention to this cell; later, Isaacs and others described it.[22]

Many other instances of significant morphological and numerical changes in the white blood cells in clinical disorders could be mentioned. However, great emphasis

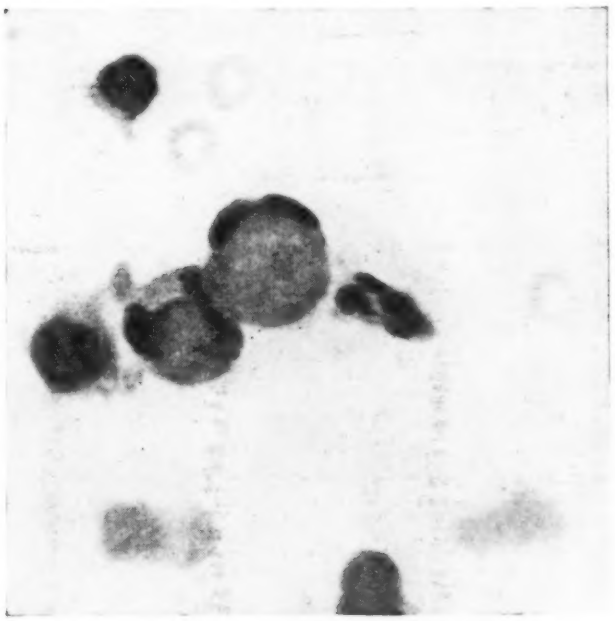

Fig. 6.—Typical lupus erythematosus cells.

has been given repeatedly to such variations, and further discussion involving such conditions as leukemia and folic acid deficiency would be of little value. Therefore, we would prefer to direct our thoughts to another type of evaluation of white blood cell disorders, namely, histochemical variations. Our laboratory has been particularly interested in the histochemical changes in white blood cells for several years. Many observations by various investigators have been made of the histochemical

constitution of white blood cells. Valentine [23] (1951) recently reviewed the many valuable contributions in this field. We shall attempt to describe in some detail the general conclusions our laboratory has been able to reach in regard to the pattern of the histochemical structure in myeloproliferative disorders of unknown causation and leukocytoses.[24] Our approach has been to attempt to determine whether morphologically indistinguishable white blood cells show variations in their content of certain chemicals and/or enzymes in cases of different clinical disorders. Our studies have included determinations of the leukocytic content of histamine, alkaline and acid phosphatase, and glycogen. Some definite patterns with respect to these three substances have been established. Chronic myelocytic leukemia is characterized by high histamine and low alkaline phosphatase and glycogen values, whereas polycythemia vera, when associated with elevated white blood cell counts, is accompanied with an elevated histamine value along with high alkaline phosphatase and glycogen levels. This has been true, irrespective of therapy or the stage of the disease; and the pattern persists in cases of polycythemia vera, even in cases in which transition to myelocytic leukemia is suspected on clinical and morphological grounds. Myeloproliferative disorders other than chronic myelocytic leukemia and polycythemia vera with leukocyte abnormalities have been found to show no constant pattern, although, in some cases, the pattern closely resembles that seen in cases of polycythemia with leukemoid features, and in others, that of chronic myelocytic leukemia. These findings suggest the heterogeneity of this poorly understood category of myelofibrotic disease. On the basis of these biochemical patterns, it has been possible, at times, for us to recognize the true nature of some of the disturbances when it would not have been possible to do this with other data. Figure 8 depicts our findings in these various disorders.

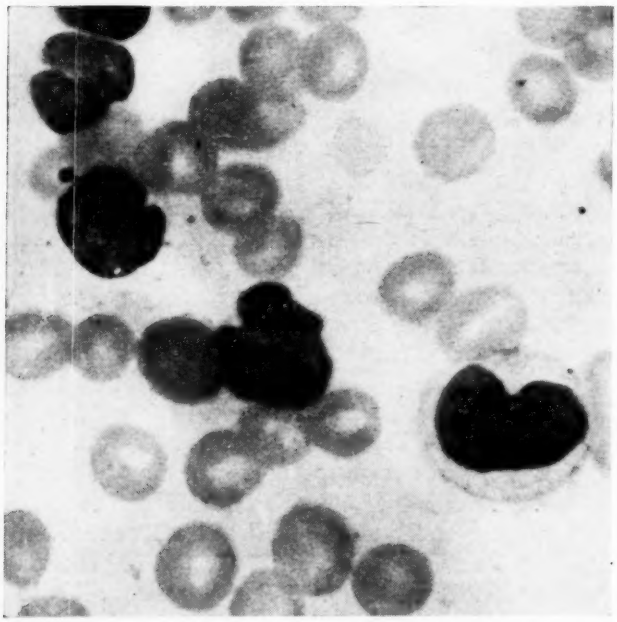

Fig. 7.—Typical lymphosarcoma cells in peripheral blood smaer.

Much more work is needed in this field, but it is readily apparent that the biochemical patterns are of distinct importance for the determination of the true nature of these disorders.

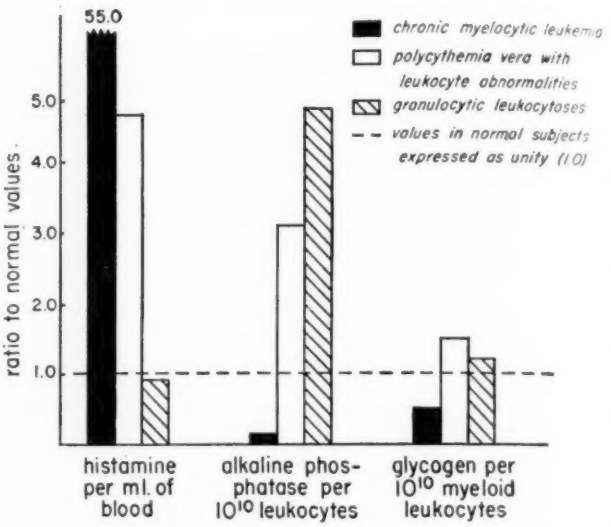

Fig. 8.—Biochemical patterns of the leukocytes in cases of chronic myelocytic leukemia, polycythemia vera associated with elevated white blood cell count, and granulocytic leukocytoses compared with those in the normal subject.

SUMMARY

The occurrence of numerical and morphological variations in white blood cells in many clinical disorders is discussed. These variations are of distinct importance in some of these pathological conditions. Biochemical patterns of the leukocytes in certain diseased states are delineated, and the possibility of the establishment of further significant patterns in other diseases is raised.

405 Hilgard Ave. (24).

Prevention of Syphilis.—It has . . . been demonstrated that the "prophylactic" treatment of syphilis during the incubation period with a single injection of 2.4 million units of procaine penicillin in oil with 2 per cent aluminum monostearate (PAM), will effectively prevent the development of syphilis in almost 100 per cent of the individuals. From the public health point of view, there is no doubt that the treatment of all syphilis contacts is indicated, since this would serve to reduce the incidence of new clinical infections. There is, however, disagreement as to the management and follow-up of these individuals. Communication with several leading syphilologists revealed that it was customary to ask these contacts to return for a serologic recheck at one to 3 month intervals for one year following completion of therapy. Moreover, spinal fluid examinations were rarely done. Yet, if that same patient had been seen one week later, at which time there might have been clinical and/or serologic evidence of early syphilis, the patient would receive similar or more therapy but methods would be enforced to have the patient return for clinical and serologic rechecks. He would also have at least one spinal fluid examination. If contacts are to be treated prior to the development of clinical and serologic manifestations, they are entitled to the same follow-up and enforced protection as the individual with proved early syphilis . . . to detect and treat possible relapses and reinfections.—C. R. Rein, M.D., and G. H. Kostant, M.D., New York, N. Y., Special Diagnostic and Therapeutic Problems in Syphilis, *American Journal of Syphilis, Gonorrhea, and Venereal Diseases*, July, 1952.

SELECTION OF PATIENTS FOR SURGICAL PROCEDURES IN CHRONIC SUPPURATIVE OTITIS MEDIA

Kinsey M. Simonton, M.D., Rochester, Minn.

During the past 15 years there has been a marked decrease in the number of patients who have required surgical procedures for treatment of inflammatory disease of the temporal bone. This decrease is the result of the profound influence that treatment with the sulfonamide and antibiotic drugs has exerted on acute inflammation of the middle ear and mastoid. The result of decrease in the incidence and destructive effect of acute infection is seen in lessening of the incidence of chronic inflammation in these regions. There remains, however, a considerable reservoir of patients who suffer from the effects of chronic suppuration of the ear that had its inception in the preantibiotic era. In addition, there are patients who currently undergo chronic inflammation of the ear as a result either of infection by resistant strains of micro-organisms or of inadequate treatment of acute infections.

The predominant factors in the production of chronic inflammatory disease of the middle ear and mastoid are destruction of tissue and the presence of stratified squamous epithelium in an abnormal location. The exception is the occasional patient with chronic inflammation in the cells of the mastoid.

Acute bacterial infection of tissue usually is found only as a temporary complication of the chronic process. For this reason, chemotherapy or antibiotic therapy offers little aid except as an adjunct to established procedures for cleansing, exposing, and draining the involved area.

CLASSIFICATION OF CHRONIC SUPPURATIVE OTITIS MEDIA

The possible variations that may be encountered in cases of chronic suppurative otitis media are infinite. A classification of these cases is of tremendous value when it is able to indicate the nature and extent of the pathological process and to suggest those measures that are appropriate for its treatment. I wish, therefore, to reiterate a simple, empirical classification of cases of chronic suppurative otitis media that has proved its value during the 30 years that it has been used at the Mayo Clinic. The classification has been presented previously by Lillie,[1] in 1928, and by Williams,[2] in 1936.

In this classification all cases of chronic suppuration of the middle ear and mastoid are divided into four groups, designated by numbers 1 to 4. Complications, whether present or impending, are, in addition, designated by appropriate descriptive terms.

Group 1.—This group comprises those patients with mucoid discharge that arises in the eustachian tube. There is no odor. The drainage may be continuous or there may be long periods of freedom from discharge. Exacerbations or recurrences usually result from acute infections of the upper part of the respiratory tract. The perforation in the tympanic membrane may be of any size or location but is usually found in the anteroinferior quadrant. The tympanic mucosa presents a normal appearance in those patients in whom it can be seen. There is no evidence of cholesteatoma or of hyperplastic change suggesting necrosis of the bone. Roentgenograms may show moderate sclerosis of the mastoid process.

Treatment is directed toward healing the eustachian tube and the elimination of abnormalities in the nose and nasopharynx. After secretions have been removed from the ear by suction through a fine cannula, liquid medication is forced through the eustachian tube from the ear. Solutions of various sulfonamides and antibiotics, liquid antiseptics, and mild solution of protein silver, have all proved effective. The use of solutions of drugs in hygroscopic glycerin-base vehicles is preferred to administration of aqueous solutions of the medicaments. Avoidance of excessive pressure when blowing the nose is useful in preventing recurrences.

Group 2.—This group includes patients who show evidence of disease in the middle ear in addition to the finding in group 1 patients. The discharge is mucoid or purulent and may have considerable odor, owing to the action of saprophytic bacteria. Polyps are often present; they may arise from the promontory of the cochlea, the annulus tympanicus, or the attic. There may be necrosis of the ossicles. Roentgenographic findings are similar to those encountered in patients in group 1. The odor of the secretion usually disappears after a day or two of treatment.

Treatment is similar to that administered to patients in group 1. Complete cleansing of the middle ear is of paramount importance and should be done daily. Polyps should be removed if they cause retention of secretions. This may be done by the use of cutting forceps or chemical cautery. Avulsion of polyps is dangerous, especially when the polyps arise from the promontory. Adequate anesthesia, either local or general in character, is essential if the surgeon is to avoid injury to the facial nerve or stapes during removal of polyps. Chemical cautery may be used successfully without anesthesia. Solutions of antiseptic or antibiotic agents in hygroscopic base are useful when kept in continued contact with the middle ear.

Group 3.—This group includes patients with a definite defect into the attic. This defect may be in Shrapnell's membrane, or it may be located in the roof of the external auditory canal at the annulus tympanicus in such fashion that the tympanic membrane remains virtually intact. Small perforations are more significant than large ones. The discharge is purulent and fetid. Granulations are frequently found. Desquamated epithelium may be found by probing or by irrigation. Loss of hearing of the stapes-fixation type is common. The

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From the Section of Otolaryngology and Rhinology, Mayo Clinic.

Read before the Section on Laryngology, Otology and Rhinology at the 101st Annual Session of the American Medical Association, Chicago, June 11, 1952.

1. Lillie, H. I.: Empirical Clinical Classification of Chronic Suppurative Otitis Media, Atlantic M. J. **31**: 559-564 (May) 1928.

2. Williams, H. L.: Classification and Management of Chronic Suppurative Otitis Media, J. Iowa M. Soc. **26**: 346-352 (July) 1936.

roentgenographic findings are similar to those found in patients in group 1 or 2. Sometimes a small area of decreased density may be found in a sclerotic mastoid.

The patients included in group 3 usually present borderline surgical conditions. If care is taken when polyps are removed, sufficient exposure may be attained to allow adequate cleansing of the attic. The attic is cleaned daily by irrigation with alcohol through a Hartmann cannula. It is then dried by means of air blown through the same cannula. The area of the perforation may then be dusted with powder consisting of a mixture of a sulfonamide with penicillin, or it may be treated with the solutions mentioned in the therapy of patients in groups 1 and 2. In those patients in whom adequate access to the attic allows thorough cleansing of this space, treatment usually results in cessation of discharge. It is often necessary to repeat the treatment at intervals of 6 to 12 months. Failure to attain relief from the symptoms after a reasonable trial of conservative therapy is indication for surgical intervention.

Group 4.—This group comprises those patients in whom there is definite indication for early operation. The objective findings are similar to those encountered in patients in group 3. Discharge is purulent, fetid, and persistent but may be small in quantity. In addition, there is a definite clinical or roentgenographic evidence of cholesteatoma. Polyps may be particularly prominent. When the patient displays evidence of labyrinthine, intracranial, or septic complications, he is immediately classified in group 4. These complications are denoted by a history of vertigo, headache, pain, convulsions, stupor, nausea and vomiting, facial palsy or septic fever, and evidence of increased intracranial pressure or a fistula into the labyrinth. Treatment in these cases is surgical.

SURGICAL TREATMENT OF CHRONIC SUPPURATIVE OTITIS MEDIA

Having decided which patients must undergo surgical treatment for chronic suppuration of the ear and temporal bone, the physician must then decide what surgical procedure is best suited to the needs of the patient. An attitude of flexibility should be maintained in the choice of surgical procedure, and the selected procedure should be adapted to the anatomic and pathological findings in the individual patient. Many of the details of the procedure will be dictated by the findings after exposure of the field of operation; however, it is permissible to discuss the broad aspects of surgical treatment and to outline the general rules for treatment of various conditions that are found associated with otic suppuration.

Whether the incision is endaural or postauricular is a matter of the preference of the surgeon. With few exceptions, any procedure on the temporal bone may be performed adequately through either approach. My personal preference is for the postauricular approach to the temporal bone for all patients except those in whom the disease process is limited to the epitympanic space and mastoid antrum. Patients with small cholesteatomas are also excepted. The comprehensive exposure of the field afforded by the postauricular incision is of special value in patients for whom extensive dissection of the mastoid process is required.

The decision as to whether to preserve the tympanic membrane and ossicles depends on several important factors: the capacity of hearing, the condition of the drum, and the extent of the pathological process in the tympanic cavity and epitympanic space. Asherson [3] reported that the average loss of hearing in patients presenting chronic otorrhea with granulations, polyps, or cholesteatoma was 40 to 45 db. for the conversational range before operation, and 50 to 60 db. after radical mastoidectomy. This indicates a loss of 10 to 20 db. incident to operation. The degree of loss of hearing after operation is much less if the drum and ossicles are preserved; therefore, the modified operation is preferable when useful hearing is present before operation. Large perforations of the tense portion of the tympanic membrane are usually accompanied by continued otorrhea after modified radical mastoidectomy. The presence of granulations, cholesteatoma, or bony necrosis in the tympanic cavity is indication for the classic radical operation. When the posterior wall of the membranous external auditory canal is kept intact until the site of disease is exposed, the decision concerning choice of operation can be delayed until the extent of disease has been fully determined.

Cholesteatosis is the condition most frequently encountered during operations for chronic mastoiditis. The operation required for treatment of this condition is tympanomastoidectomy or one of its variations. The essential feature of the operation is exteriorization of the cavity, and at completion of this procedure the walls of the cavity should be smooth and free of pockets or overhanging ridges of bone. All areas should be readily accessible for cleaning through the external auditory canal. To accomplish these objectives it is necessary to lower the posterior wall of the external auditory canal and to remove the lateral wall of the epitympanic space. Opinion varies on the advisability of preserving the matrix of the cholesteatoma to serve as a graft in the cavity. Continued formation of cholesteatoma has been observed in cases in which the matrix was retained. The matrix is removed from patients operated on at this clinic.

Chronic inflammation in a cellular mastoid requires complete exenteration of the cellular system. The mastoid antrum and epitympanic space should be adequately exposed, since chronic inflammation of the mucosa is present in these locations. Some patients may have satisfactory results after the complete mastoid operation, but the percentage of failures is definitely decreased by use of the method in which the cavity is exteriorized by means of a modified radical operation.

Phlebitis or thrombosis involving the sigmoid or superior petrosal sinus is not a frequent complication of chronic mastoiditis. Unexplained fever, usually of the septic type and accompanied by chills, should arouse suspicion of the presence of these lesions. Headache is a less frequent symptom. Culture of the blood may give positive results, particularly if it is taken when the temperature is rising during a chill. Tenderness and lymphadenopathy may be present along the course of the internal jugular vein; edema of the homolateral optic disc

3. Asherson, N.: The Radical Mastoid Operation: A Pre- and Post-Operative Audiometric Statistical Survey of Hearing Loss in Chronic Otorrhoea, J. Laryng. & Otol. **62**: 568-602 (Sept.) 1948.

may be observed; and, if the thrombus occludes the sinus, evidence of obstruction may be found by use of the Tobey-Ayer and similar tests. Examination of the cerebrospinal fluid usually gives normal results.

At operation it is commonly noted that the affected sinus is exposed by the disease process and there are granulations covering its surface. In addition to the treatment indicated for cholesteatosis, the sinus plate should be removed widely enough to expose normal-appearing dura on all sides of the lesion. The sinus should then be carefully palpated and aspirated for evidence of formation of thrombus. Treatment of sinus thrombosis formerly involved opening the sinus, removing the clot, and packing the sinus to control bleeding. The present availability of antibiotics makes more conservative treatment practical, and in most instances removal of the primary focus of infection in the mastoid, exposure of the sinus, and active antibiotic therapy should suffice to cure the infection.

Pachymeningitis results from erosion of bone overlying the dura of either the temporal lobe or the cerebellum, with resultant exposure and inflammation of the dura. Headache or pain is the most important symptom. Headache tends to be most severe in the early morning hours, awakening the patient. The pain is not localized to the region of the ear, but usually is on the same side as the lesion. History of headache that increases in severity when drainage from the ear decreases is particularly significant and requires early surgical intervention. At operation the mastoid is exposed and cleaned out as for cholesteatosis. Bone is then removed from the margins of the region of inflamed dura until normal dura is exposed on all sides of the lesion. Active antibiotic therapy is indicated to prevent extension of the infection. In cases in which the dura has not been grossly exposed by the disease, purposeful exposure and investigation of the dura are indicated.

Subdural or contiguous brain abscess may be effectively treated through the mastoid incision. The diagnosis of these lesions is too broad a subject for discussion here. At operation an area of dura covered with granulations is found. The dura is under increased tension and does not pulsate. Careful observation often reveals pus welling up from a fistula in the dura. After wide exposure of the dura, as described in the treatment of pachymeningitis, the dura may be incised and the pus evacuated from the subdural space. Brain abscess contiguous to the dura may be treated by the same route. Current neurosurgical opinion favors early treatment of brain abscess prior to the formation of a capsule. The abscess is evacuated and necrotic brain tissue removed by suction. The abscess cavity is then filled with a solution of penicillin, the dura is closed, and vigorous antibiotic therapy is instituted. It is safer to treat brain abscess that is not contiguous to the mastoid cavity through a clean incision located away from the mastoid.

Fistula of the labyrinth, sometimes called "perilabyrinthitis," results from erosion of the bony wall of one or more of the semicircular canals, usually as the result of an expanding cholesteatoma. The presence of intermittent vertigo calls attention to this complication. Presence of the fistula is demonstrated by the induction of nystagmus when pressure within the external auditory canal is altered. The lesion is treated by removal of the overlying cholesteatoma or granulations. Granulations lying directly in the fistula are not disturbed.

Suppurative labyrinthitis is manifested by loss of cochlear and vestibular function following an episode of severe labyrinthine irritation. Acute labyrinthitis is treated expectantly with adequate chemotherapy and complete rest. Tests of vestibular function are diligently avoided. The occurrence of meningitis, or of symptoms that suggest impending intracranial complication, is indication for surgical drainage of the labyrinth. Tympanomastoidectomy without labyrinthectomy should be done in those patients who recover from labyrinthitis without complications. Observance of purulent drainage from a nonfunctioning labyrinth during performance of tympanomastoidectomy indicates need for drainage of the labyrinth. The procedures for drainage of the labyrinth have individual points of merit. It is important that both the vestibule and the cochlea be adequately exposed and that suitable precautions be observed to preserve the integrity of the facial nerve.

Infection of the petrous pyramid varies considerably in its symptoms and may tax the diagnostic acumen of the otologist. The most frequent symptom is pain in the area of distribution of the fifth cranial nerve. Any branch may be affected, but pain is commonest in or around the orbit. The sixth, seventh, and eighth cranial nerves may also be affected by petrosal lesions. Low-grade sepsis is usually seen. Persistent drainage through the mastoid or middle ear is common, although the abscess may break through the anterior surface into the carotid canal, thus producing Horner's syndrome. The abscess may also break through the posterior surface, causing symptoms of lesions of the posterior fossa, or through the inferior surface, producing abscess in the nasopharynx. The surgical approach to infections in the petrous pyramid is made after preliminary tympanomastoidectomy. The labyrinth is skeletonized and a thorough search is made for cell tracts or fistulas in the region surrounding the labyrinth. The region at the mouth of the eustachian tube should be closely searched. The enlargement of any cell tract or fistula may result in drainage of the abscess. If no preformed tract is found, the apex of the petrous pyramid may be entered through the carotid canal as described by Ramadier [4] and by Lempert.[5] This approach is particularly valuable when the symptoms and roentgenologic examination suggest the presence of a lesion in the anterior or inferior aspects of the petrous apex.

Paresis or paralysis of the area supplied by the facial nerve that occurs in association with chronic suppuration of the temporal bone is a definite indication for operation. Preparatory tympanomastoidectomy is done, and the pathway of the nerve is explored for evidence of pressure resulting from the infection. The most vulnerable region is the horizontal portion of the nerve that traverses the middle ear. Cholesteatoma and granulations are carefully removed from the nerve. When the nerve

4. Ramadier, J.: Exploration de la pointe du rocher par la voie du canal carotidien, Ann. d'oto-laryng. pp. 422-444 (April) 1933.

5. Lempert, J.: Complete Apicectomy (Mastoidotympanoapicectomy): A New Technic for the Complete Exenteration of the Apical Carotid Portion of the Petrous Pyramid, Arch. Otolaryng. 25: 144-177 (Feb.) 1937.

appears swollen, it is decompressed by removal of the walls of the fallopian aqueduct proximal and distal to the exposed area until normal-appearing nerve is encountered.

SUMMARY

The simple, empirical classification of cases of chronic suppurative otitis media presented at once suggests the nature and extent of the pathological process and indicates appropriate measures for treatment in the individual case. A brief description is given of the salient clinical features that allow cases of chronic suppurative otitis media to be classified in the various subdivisions. The application of this scheme for the proper selection of surgical procedures is described. The surgical treatment of various types of chronic suppurative otitis media and its complications is discussed.

POLLEN AND MOLD ALLERGY IN THE SOUTHWEST

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There are a number of problems concerning air-borne allergens peculiar to the Southwest. These are here presented in the form of general observations with the purpose of acquainting allergists of other areas, that they may be better able to advise their patients migrating to or visiting this region.

Geographically, the Southwest is west of a fairly straight line dropped due south from Omaha or Des Moines into the Gulf of Mexico. This line, passing to the east of Tulsa, Okla., and about midway between Dallas and Houston, Texas, is the 30 in. annual rainfall line. The east-west line is a variable curve, varying from year to year, below which there are late freezes and frosts, long hot summers with little rainfall, and short mild winters with temperatures rarely going below 20 F for a day or two at a time. Rainfall is rather concentrated in early spring and fall, with occasional thunder showers. During the winters warm sunshine frequently runs the daily temperature into the 70's or 80's.

Conditions are in no wise exactly similar throughout this area of about 1,000 miles in diameter. In its northeastern portion there is a mild resemblance to the central and eastern United States in weather and pollination, whereas, in the southern part, in the lower Rio Grande Valley, winters often come and go with neither frost nor freeze.

In this arid Southwest, spring is ushered in by elm, cottonwood, and hackberry in late February or early March; oak in March, followed by pecan and mesquite in April. Elm, oak, pecan, and mesquite are the more important, owing to their longer seasons of activity. During mild winters the cold does not break the dormancy, and this has a tendency to lengthen the duration of the flowering period for some trees. Mesquite (Prosopis juliflora with its related species) is indigenous to the Southwest, wide in distribution, and peculiar in that it will pollinate after showers and warm weather at any time of year, even at times in the late fall and winter. Often it may be seen flowering while bearing its characteristic beans in the fall.

Ligustrum (Ligustrum japonicum), widely used as a yard shrub, hedge, and tree, is a heavy pollinater; however, it is not widely wind-borne, owing to the large sticky granules, but does produce symptoms in persons living in close proximity.

Grasses may bloom at any time, with peaks of pollination in April, May, and June and again in September and October. Often the fall grass counts exceed those of ragweed. Bermuda (Cynodon dactylon) and Johnson (Sorghum halepense) grass are the chief offenders. Timothy is rare or unknown except along the eastern borders of this area, and its extract is not diagnostic in or effective therapeutically for patients sensitive to Bermuda and Johnson.

Weeds of many varieties abound especially in disturbed soil, fence rows, and creek and river bottom lands. Most are poor pollinaters, causing no respiratory disease, but many of the poor pollinaters cause contact dermatitis. One, indigenous to the extreme southern part, Parthenium hysterophorus (wild feverfew, Mexican birdseed weed) has spread north to Kansas City and St. Louis and causes almost as much dermatitis as does ivy. Rough pigweed of the amaranth family may start blooming in February, while careless weed (Amaranthus palmeri) usually starts in May. These usually die down and become inactive in July and August but, if summer showers occur, may remain active and cause much trouble from May to November or December frosts. In irrigated orchards, careless weed is used as a cover crop, and, if no frost occurs, pollen may be in the air virtually all year. Another species of amaranth (Amaranthus graecizans) is a tumbleweed of the western plains—not to be confused with the real tumbleweed or Russian thistle (Salsola pestifer) well known in the West. Salsola supersedes all other pollinaters in the more arid prairies of western Texas, Arizona, New Mexico, western Oklahoma, parts of Kansas, and Colorado. The pollen is highly antigenic and active from May or June until frost. Burweed marsh elder (Iva xanthifolia) is found in the northwest and swings down from the northwest into the western areas, and marsh elder (Iva ciliata) is present in the eastern portion of the Southwest.

The other summer weeds of importance are false ragweed (Franseria tenuifolia—San Antonio to the north and west—and Franseria acanthicarpa—from San Antonio and west) and sages. Franseria, pollinating from May until frost, is not related antigenically to the ambrosias, although its appearance is similar to that of common ragweed and is often mistaken for it. Prairie sage (Artemisia gnaphalodes) and sagebrush (Artemisia tridentata) are not heavy pollinaters but not infrequently produce hot sensitivities. Senisa (Leucophyllum texanum), a

Read before the Section on Miscellaneous Topics: Session on Allergy at the 101st Annual Session of the American Medical Association, June 11, 1952.

plant widely used along highways and yards as a decorative shrub, causes an occasional sensitivity.

Ragweeds cannot be placed in the prime position they hold elsewhere. Cases of pure ragweed sensitivity are of somewhat infrequent occurrence; multiple seasonal or perennial cases are of high frequency. Even patients who have only fall hayfever are usually also sensitive to scrub elm or cedar elm (Ulmus crassifolia), a fall pollinating red-berried cedar (Juniper pinchotii), an Amaranth, or other pollinaters active in August, September, and October and have to be treated against these as well as ragweed. Western ragweed (Ambrosia psilostachya) is often observed in active bloom from May through December and in excessively dry years may grow only 4 to 6 in. (10 to 15 cm.) high. The giant ragweed (Ambrosia trifida and aptera [1]) will attain a height of 10 to 12 ft. (305 to 366 cm.) along the roadsides and is one of the chief pollen contributors in the Southwest. Ragweed counts, except in the Dallas area north and eastward, run rather low, with counts in some seasons and areas from 0 to only 10 or 20 a day. Many persons who have severe symptoms in the Northeast are free of ragweed discomfort in the Southwest but, of course, have the usual tendency to become sensitized to Russian thistle or mountain cedar within a few years.

When plant activity falls to nothing elsewhere, the Southwest has mountain cedar, a heavy pollinater that starts in December and continues into March. The cedar area is some 500 miles in diameter in central and northern Texas. This pollen will blow 300 miles in sufficient quantity to cause trouble. In the cedar ranges the daily pollen counts go into the thousands, and patients are difficult to protect.

With the scant rainfall, I expected in my early studies to discover the air-borne molds to be of little importance. I have found none of the Southwest exempt from mold-sensitive patients. There are numerous wells, windmills, and open tanks used to water sheep and cattle throughout the area, residents in the small villages water their lawns and shrubs; there are numerous irrigated farming projects; and coastal fogs roll far inland. Thus, enough moisture prevails to give a rather high mold incidence. Alternaria, which likes the bark of the mesquite (which covers about 8,500,000 acres), as well as other dead vegetative material, has its spring and fall peaks, and Helminthosporium, whose favorite host is winter oats, is perennial. These two are the most frequent offenders, followed by Hormodendrum, Spondylocladium, Phoma, and Rhizopus. I think all varieties of air-borne molds have been found in the arid Southwest. Roughly, I approximate 5% of the inhalant-sensitive patients are clinically mold sensitive, with skin reactivity evident in about 20%.

In general summary, the Southwest has longer growing seasons with smaller daily pollen counts than elsewhere. Single seasonal patients are exceptional, and cases of multiple and perennial sensitivity are of high incidence. Whereas allergists in other areas can best vacation in the winter, those in the Southwest vacation in July and August, when it is usually very dry and plant activity is often nil. My impression is that patients in the Southwest are, in general, less sensitive than elsewhere and, therefore, require heavier concentration of extracts for diagnosis and larger doses for treatment. Certainly small dosage therapy is a failure in the Southwest.

705 Houston St. (5).

1. Aptera or blood weed or southwestern giant ragweed.

AUREOMYCIN IN MUMPS

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Although mumps is a self-limited and usually a benign disease, it can cause a prostrating illness in the man past puberty. The complications of orchitis, meningo-encephalitis, and pancreatitis occur in 30 to 50% of adult men with epidemic parotitis. Therefore, any therapeutic agent that shows promise of permitting the patient to return to full activity at an earlier date is worth evaluating.

There have been several reports suggesting that aureomycin may be effective in treating mumps. Langley and Bryfogle reported three patients with uncomplicated mumps in whom they felt that aureomycin significantly shortened the period of morbidity.[1] Schmuttermeier and associates reported one patient with orchitis,[2] and Spinelli and co-workers reported four patients with orchitis in whom aureomycin seemed to shorten the febrile course and period of incapacity.[3] Schaub reported a series of 17 patients treated with aureomycin whom he compared with a similar group treated symptomatically in previous years. He felt that aureomycin prevented the complications of mumps and reduced the severity of orchitis and pancreatitis in patients in whom these complications occurred.[4] On the other hand, unfavorable reports are limited to the failure to prevent mumps in two patients in spite of treatment with aureomycin during the incubation period [5] and the apparent lack of response to aureomycin in a 4-year-old boy with mumps.[6]

In using another broad spectrum antibiotic, chloramphicol (chloromycetin®), Nickerson and Worden [7] were unable to demonstrate any beneficial results in 57 patients with mumps. Since there have been no controlled studies, in order to evaluate the efficacy of aureomycin in treating mumps we have conducted a controlled series. The presenting complaint in all patients was swelling of

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1. Langley, W. D., and Bryfogle, J.: Aureomycin in Epidemic Parotitis, J. A. M. A. **143**: 1333 (Aug. 12) 1950.

2. Schmuttermeier, E. W.; Suroboda, W., and Thalhammer, O.: Aureomycin bei kompliziertem Mumps des Erwachsenen, Wien. klin. Wchnschr. **62**: 979 (Dec. 29) 1950.

3. Spinelli, N. P. R.; Cressy, N. L., and Kunkel, P.: Aureomycin in the Treatment of Mumps, Orchitis and Encephalitis, Connecticut M. J. **15**: 113 (Feb.) 1951.

the parotid gland. As the patients were admitted to the acute contagious disease section they were alternately placed on symptomatic therapy alone or symptomatic therapy plus aureomycin. The aureomycin dosage was 500 mg. four times a day for 12 doses if the patient was afebrile. In patients who continued to be febrile or later developed febrile complications aureomycin was continued or begun again at the same dosage level until their temperature remained normal for 24 hours.

TABLE 1.—*Results of Serum Amylase Therapy in Forty-Six Patients with Epidemic Parotitis*

	Elevated 200 Units and Over	Less Than 200 Units
No complication	13 (28.2%)	17 (37%)
Complicated by orchitis or meningoencephalitis	7 (15.2%)	9 (19.6%)

TABLE 2.—*Average Course of All Patients*

	Parotid and/or Submaxillary Swelling, Days	Febrile Days	Hospital Days	Total Illness Days
Aureomycin treatment (24 patients)	8.1	4.38	9.65	10.8
Symptomatic treatment (24 patients)	9.83	3.4	10.3	11.3

All patients were treated identically except for aureomycin therapy. All were treated by bed rest with bathroom privileges only, and scrotal supporters were issued to all patients. Diethylstilbestrol, in doses of 5 mg. three times a day, was given to all patients with orchitis until they were afebrile for 24 to 48 hours. The patients were kept in the hospital until all evidence of glandular involvement subsided.

All patients in the study group were adult men between the ages of 17 and 25 years. There were 24 patients in each group. Serum amylase determinations were performed on all but two patients. The determinations were of no value in indicating the severity of the disease or in prognosticating the likelihood of developing complications (table 1).

TABLE 3.—*Duration of Total Illness*

Days	Aureomycin Treated Patients	Symptomatically Treated Patients
3- 5	2	1
6- 8	3	3
9-11	10	10
12-14	6	6
15-17	2	4
18-20	1	0

TABLE 4.—*Complications in Relation to Type of Therapy*

	Aureomycin Treated, 24 Patients	Symptomatically Treated, 24 Patients
Orchitis within 24 hours of admission	3	2
Orchitis after 1 day of hospitalization	6	3
Meningoencephalitis	0	2

4. Schaub, F.: Aureomycin beim Mumps des Erwachsenen, Praxis **40**: 711 (Aug. 30) 1951.
5. Mazursky, M. M.; Wright, L., and Weichsel, M.: Clinical Observations on Aureomycin in Varicella, Pediatrics **5**: 276 (Feb.) 1950.
6. Shane, S. J., and Sodero, S. W.: Aureomycin and Mumps, Canad. M. A. J. **63**: 387 (Oct.) 1950.
7. Nickerson, G., and Worden, E. M.: Chloromycetin in the Treatment of Mumps, Canad. M. A. J. **66**: 17 (Jan.) 1952.

RESULTS

Those patients treated with aureomycin averaged 8.1 days of glandular swelling of the parotid and/or submaxillary glands, while those treated symptomatically averaged 9.3 days of swelling. Of the patients who were febrile, counting the total duration of the febrile period with or without complications, those treated with aureomycin averaged 4.4 days of temperature elevation, while those not receiving aureomycin averaged 3.4 days. The total hospital stay and the total duration of illness were similar in the treated and untreated groups (table 2). The distribution of patients according to the total duration of illness was almost identical in the aureomycin and in the symptomatically treated groups (table 3). The median duration of illness in the aureomycin treated group was 10 days and in the symptomatically treated group 11 days.

Orchitis developed in six patients who were given aureomycin after they had been in the hospital for more than 24 hours, and, in three patients, it developed during the first 24 hours after admission. There were seven patients with complications in the group treated symptomatically; meningoencephalitis developed in two patients; two had orchitis on admission; and in three, orchitis developed after they had been hospitalized for more than 24 hours (table 4).

TABLE 5.—*Average Course of Patients with Orchitis*

	Testicular Swelling (Days)	Fever with Orchitis (Days)	Hospitalization (Days)	Illness (Days)
Aureomycin treated, 24 patients	8.5	4.2	12.5	13.5
Symptomatically treated, 24 patients	8.4	4.6	11.6	12.2

In the patients in whom orchitis developed, the men receiving aureomycin averaged 8.5 days of testicular swelling, and those treated symptomatically averaged 8.4 days. The average duration of temperature elevation during the period of orchitis was 4.2 days in those receiving aureomycin and 4.6 days in those receiving symptomatic therapy. The average duration of hospitalization and total illness was similar in the two groups (table 5).

In two patients who were treated symptomatically, signs of meningeal irritation developed. The diagnosis of meningoencephalitis was confirmed by lumbar puncture, the cerebral spinal fluid showing 402 cells with 88% lymphocytes and 402 cells with 99% lymphocytes, respectively. Neither patient was more than moderately ill, and they were afebrile after three and two days, respectively, and were asymptomatic after 72 hours of illness. It took approximately 10 days for the spinal fluid count to return to normal.

Pancreatitis did not develop in any patient in this study. One patient emphasized that aureomycin therapy in itself may not be without risk, as it permits aureomycin resistant organisms to multiply and cause disease. A 21-year-old man was admitted to the hospital with parotid swelling and was placed on aureomycin therapy. Orchitis developed on the fifth hospital day, and he had a temperature of 103 F. He was restarted on aureomycin, 500 mg. four times a day, as soon as it became obvious that orchitis had developed. On the seventh day after orchitis developed, while still on aureomycin, a severe sore throat developed, with multiple pinhead size, yellowish spots

over the entire mucosa of the oropharynx. Culture revealed hemolytic Staphylococcus aureus that proved to be resistent to aureomycin, penicillin, streptomycin, and terramycin but was moderately sensitive to chloramphenicol. The patient made an uneventful recovery after the aureomycin was discontinued. He was treated with local 2% aqueous methylrosaniline chloride (gentian violet) and chloramphenicol. His total hospital stay was 18 days. The last six days of his hospital stay was required for treatment of his oropharyngitis, which was probably a direct complication of the aureomycin therapy.

SUMMARY AND CONCLUSIONS

Two identical groups of patients, 24 patients in each, with epidemic parotitis were treated, one group, symptomatically and the other, symptomatically and with aureomycin. The patients were evaluated for the effect that aureomycin exerted on the development of complications, duration of acute febrile illness, and duration of glandular swelling. No significant differences were demonstrated on the duration of the febrile period or duration of glandular swelling. We feel that the development of any of the complications of mumps is purely fortuitous and that the incidence of two patients with meningoencephalitis in the symptomatically treated group as compared with no patients in the aureomycin treated group does not reflect any protective action of aureomycin. This lack of ability to protect against complications is further emphasized by the fact that the group receiving aureomycin had six patients in whom orchitis developed after they had had at least 24 hours of therapy, while the group treated symptomatically had five patients in whom complications developed, including the two patients with meningoencephalitis after 24 hours of hospitalization. In our study, we were unable to demonstrate that aureomycin had any beneficial effect in epidemic parotitis (mumps) or its complications.

BIOLOGICALLY FALSE POSITIVE SEROLOGIC TESTS FOR SYPHILIS

TYPE, INCIDENCE, AND CAUSE

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and
Charles F. Mohr, M.D., Baltimore

The Wassermann test for the diagnosis of syphilis was introduced into clinical practice in 1907.[1] This immunologic reaction, utilizing the phenomenon of complement fixation, has since been modified, refined, and simplfied through the use of flocculation techniques (Michaelis [2]). Many improvements of original techniques have been made by subsequent workers, resulting in the introduction of new tests usually known by the names of their originators, e. g., in the United States, the Kolmer, Eagle, Kahn, Kline, Hinton, Mazzini, and other tests, or even subvariants of these, as the Kahn standard, presumptive, and verification tests. Although it is customary for each author-serologist to claim that his test has some special virtues that set it apart from others, it is none the less true that all of these tests depend on basically identical physiochemical and immunologic phenomena. They differ from each other only in minor technical details. It is also true that in a very real and important sense, and contrary to the generally prevailing impression, all of these tests are nonspecific.

NONSPECIFICITY OF STANDARD SEROLOGIC TESTS [3]

Antigen.—The antigen employed in present day standard serologic tests for syphilis is an alcoholic lipoid extract of various normal animal (or even fish or plant) tissues, usually beef heart. It has been purified to various degrees by many workers, with the final demonstration by Pangborn [4] that the active antigenic component of such beef heart extracts is a chemically definable substance, cardiolipin.

In infectious diseases other than syphilis (or other treponematoses), antigens designed to demonstrate antibody response in vivo are directly extracted from the particular etiological organism or virus. Antigens used in the standard serodiagnosis of syphilis are unique, however, in that they do not derive from T. pallidum but from tissue extractives of animal or other species that themselves are usually not susceptible to infection with that organism.[5] These antigens are therefore nonspecific in the usual immunologic sense.

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This investigation has been supported by grants-in-aid from the National Institutes of Health, United States Public Health Service.

Figures 3 and 4 were reproduced by permission of Drs. R. A. Nelson and H. E. Zellman. The figures have not been published previously.

1. Wassermann, A.: Über die Entwicklung und den gegenwärtigen Stand der Serodiagnostik gegenüber Syphilis, Berl. klin. Wchnschr. **44**: 1599, 1634, 1907.

2. Michaelis, L.: Präcipitinreaktion bei Syphilis, Berl. klin. Wchnschr. **44**: 1477, 1907.

3. Our immunologist colleague, A. G. Osler, commented in a personal communication on this question of specificity as follows: "In a strictly immunologic sense, the adjective 'specific' is limited to the disproportionately unique reaction between an antibody and the antigen used to stimulate the immune response. The same antibody may however, and usually does, react with other antigens whose chemical structures are in some way similar to the homologous antigen. Thus, the serum of a rabbit immunized with Type III pneumococci will react best with the capsular polysaccharide of this organism. This serum will also react in varying degree with the capsular polysaccharide of the Type VIII pneumococcus, as well as with other substances such as the extracted polysaccharides obtained from cherry tree gum and oxidized cotton. The latter, heterologous reactions, were presumed to be non-specific until studies indicated a similarity in chemical architecture of the polysaccharides concerned.

"The STS reactions, therefore, may be due to an analogous cross reaction between immunologically similar antigens present in *T. pallidum* and/or human tissue, beef heart tissue, wheat germ, etc. In this sense, the STS antigens may be specific, cross-reacting antigens in the usual immunologic sense."

4. Pangborn, M. C.: A New Serologically Active Phospholipid from Beef Heart, Proc. Soc. Exper. Biol. & Med. **48**: 484, 1941.

5. Human tissues may also serve as antigen source. Moreover, since T. pallidum are not available in sufficient quantity to permit antigenic fractionation, it is not known whether the "Wassermann antigen" is actually present within the treponemes.

Antibody.—The antibody detected in syphilitic serums by these nonspecific antigens is called reagin (because it reacts). Little is known of its immunochemical constitution, except that it has a molecular weight similar to that of other antibodies and is associated with the gamma and to a lesser extent with the beta globulin fractions of serum.

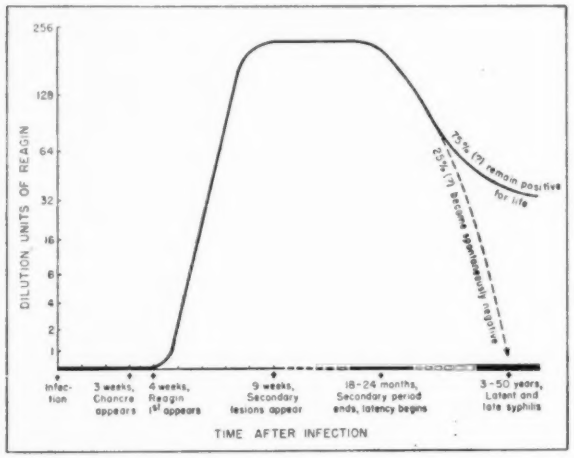

Fig. 1.—In this diagrammatic representation of the behavior of reagin in untreated syphilitic infection in man, the ordinate represents average quantitative titers in dilution units. The abscissa (broken to represent very unequal time intervals) represents duration of infection. Reagin first appears in the serum about one week after development of the chancre (about four weeks after infection); it rapidly increases in titer during the next five to six weeks, usually reaching a maximum at the time of the secondary outbreak. Thereafter, it tends to stabilize at the same level for about two years (early latency), and then in ensuing years, and on the average, to decrease in titer. In some patients, it may spontaneously disappear, even in the absence of treatment. In others, it persists (with a positive serologic test for syphilis) for a lifetime, but at a lower average titer than in earlier years. This figure is reproduced from Supplement 23 to the *Journal of Venereal Disease Information.*[12]

A great deal of information is available as to the qualitative and quantitative behavior of reagin in the presence of treponemal infection (whether it is syphilis, yaws, pinta, or bejel), both in experimental animals and man, and whether the infection is treated or untreated. Much of the information pertinent to the argument of this paper may be presented diagrammatically (fig. 1 and 2). Unfortunately, while reagin appears in considerable quantity in the serum of animals and man infected with the treponemes, it (or a similar substance) is also present in considerable amount in the serums of many animal species, such as chickens, cattle, and horses,[6] and in minute quantities in the serum of all normal human beings (Kahn[7]). In most normal human serums the amount of reagin present is so small as not to be detectable by standard serologic tests, as they are usually adjusted for sensitivity and specificity.

Unfortunately also, reagin (or a reagin-like substance) may increase in amount in the serums of nonsyphilitic persons in varying incidence, ranging from 5 to 100%, during or after a number of infections with no etiological relation to syphilis. These infections will be discussed in more detail. In a few healthy normal persons (from 1 in 3,000 to 1 in 5,000, according to Eagle[9]), therefore, and in many others under the influence of infections other than syphilis, enough reagin may be present in the serum to produce positive tests for syphilis with standard techniques. The tests in these cases are spoken of as biologically false positive tests.

Many unsuccessful efforts have been made to determine whether the reagin present in the treponematoses and in the conditions in which biologically false positive tests occur is qualitatively identical. Because of this lack of success, all "verification" procedures depending on the use of beef heart lipoid antigens, including that of Kahn[10] and the "euglobulin-inhibition" test of Neurath and his associates,[11] have no practical merit.

Frequency of Biologically False Positive Reactions.—Two factors have provided startling information that biologically false positive reactions are far more frequent than had previously been supposed. Beginning in 1938, a program of mass blood testing for syphilis has developed in the United States. In 40 states routine blood tests of all candidates for marriage and of all pregnant women are required by law. The armed services (by regulation) require such routine tests of all personnel at entrance into and again at separation from the service. In many industries, preemployment blood tests are demanded. Routine serologic testing of all patients is cus-

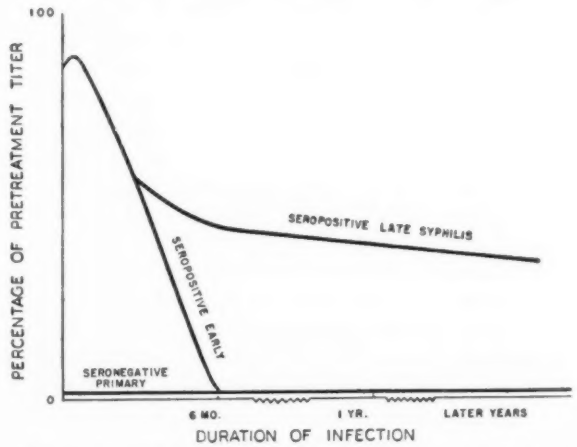

Fig. 2.—In this chart showing the usual behavior of reagin in treated syphilitic infection in man, the ordinate represents the titer at various stages as the percentage of the average pretreatment titer, and the abscissa (again broken to indicate lapse of time) the duration of infection. The curves represent the usual response to satisfactory treatment, whether it is by metal chemotherapy or penicillin. The proportions of patients in which these usual responses occur, and types of deviation from them, are discussed in various publications, particularly that of Hoekenga, Buerk, and Rider.[8] In seronegative primary syphilis, reagin, which is not detectable at the start of treatment, remains absent; the patient remains seronegative (90 to 95%). In seropositive early syphilis (primary or secondary), reagin usually disappears about six months after the initiation of treatment, or in the case of penicillin, its completion (in 70 to 80% of cases). In late syphilis of all types, the effect of treatment is usually to reduce reagin titer, but not to effect its disappearance, the patient remaining seropositive (seroresistant).

6. Kemp, J. E.; Fitzgerald, E. M., and Sheperd, M.: The Occurrence of Positive Serologic Tests for Syphilis in Animals Other than Man, with a Review of the Literature, Am. J. Syph., Gonor. & Ven. Dis. **24**: 537, 1940.

7. (*a*) Malloy, A. M., and Kahn, R. L.: The Ultramicroscopic Precipitation Reaction in Syphilis, J. Infect. Dis. **48**: 243, 1931. (*b*) Kahn, R. L.: An Introduction to Universal Serologic Reaction in Health and Disease, London, Commonwealth Fund, Oxford University Press, 1951.

8. Hoekenga, M. T.; Buerk, M. S., and Rider, R. V.: The Relationship of Early Clinical Failure to Serologic Response in Penicillin-Treated Early Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **33**: 323, 1949.

9. Eagle, H.: On the Specificity of Serologic Tests for Syphilis as Determined by 40,545 Tests in a College-Student Population, Am. J. Syph., Gonor. & Ven. Dis. **25**: 7, 1941.

10. Kahn, R. L.: A Serologic Verification Test in the Diagnosis of Latent Syphilis, Arch. Dermat. & Syph. **41**: 817, 1940.

11. Neurath, H.; Volkin, E.; Craig, H. W., and Erickson, J. O.: Biologic False Positive Reactions in Serologic Tests for Syphilis: A Preliminary Survey Analysis with the Euglobulin-Inhibition Method for the Serologic Differentiation Between True and Biologic False Positive Reactions, Am. J. Syph., Gonor. & Ven. Dis. **31**: 436, 1947.

tomary on admission to most good hospitals, and of all patients in the practices of many physicians. As a result of this program, many millions of Americans have been subjected to such routine tests, and new millions are tested annually.

The second factor is that the mobilization of about 16 million young men in World War II resulted in epidemics of infectious disease (the exanthemas of childhood, respiratory infections, malaria, infectious hepatitis, and others) under conditions in which routine, often serial, blood testing was possible in a manner not previously achieved in civilian medical practice. This combination of events provided new information as to the comparative frequency of biologically false positive reactions in the infectious diseases listed in table 1. The diseases and conditions named in the table represents an incomplete list, drawn from sources too numerous to mention individually. The most important papers are those of Moore,[12] Davis,[13] Rein,[14] and Stokes.[15] The treponematoses, yaws, bejel, and pinta (each caused by organisms morphologically indistinguishable from T. pallidum), are not included in the table. In these infections, positive serologic tests are found with the same frequency as in syphilis, and are regarded as "true positive," not biologically false positive reactions.

The approximate percentage incidence shown represents an average estimate of the incidence of positive serologic tests for syphilis in many reported series. Individual reports vary enormously, depending on the sensitivity of the particular serologic technique employed, and on whether serial testing was carried out during and after the particular infection or condition. Finally and most important, it must be remembered that the incidence of positive reactions recorded above includes some persons with syphilis as well as biologically false positive reactors. In no series so far reported for any condition (except leprosy) have the positive reactors with standard serologic tests been checked with the treponemal immobilization test, and the actual incidence of biologically false positive reactors is as yet unknown.

Attention was particularly focused on the biologically false positive phenomenon by the fact that among personnel of the U. S. Army routinely subjected to blood testing for syphilis at separation from the service at the end of World War II, no less than 75,000 persons who were known to be seronegative at entry into the service and had no record of infection with any venereal disease or of antisyphilitic treatment, were found to be seropositive! It was not possible to follow this entire group, but spot surveys of significant numbers indicated that of those rechecked as seropositive (to exclude technical error), less than one-half probably had syphilis and more than one-half probably had biologically false positive reactions. This fact, plus data derived from considerable experience in a private consultation practice, has led us [16] to express the epidemiological opinion that in certain population groups in the United States (especially in white persons of relatively high socioeconomic status in the northeastern, northern, and north-

TABLE 1.—*Approximate Incidence of Biologically False Positive Reactions in Various Nonsyphilitic Conditions*

Infections			
Disease	Approximate Incidence of BFP * Reactions, %	Disease	Approximate Incidence of BFP Reactions, %
Bacterial		**Rickettsial**	
Leprosy	60	Typhus	20
Tuberculosis, advanced	3-5	**Protozoal**	
Pneumonia, pneumococcal	2-5	Trypanosomiasis	10
Subacute bacterial endocarditis	5	**Viral**	
Chancroid	5	Vaccinia	20
Scarlatina	5	Pneumonia, "atypical"	20
Spirochetal		Measles	5
Leptospirosis	10	Chickenpox	5
Relapsing fever	30	Lymphogranuloma venereum	20
Rat-bite fever	20	Infectious hepatitis	10
Plasmodial		Infectious mononucleosis	20
Malaria	100	Common cold	? low

Noninfectious Diseases or Conditions	Approximate Incidence of BFP Reactions
Lupus erythematosus (disseminated or discoid)	20
Rheumatoid arthritis	5
Blood loss, repeated (as in multiple donations for transfusion)	? low
Pregnancy	? low

* BFP = biologically false positive.

12. Moore, J. E.: The Diagnosis of Syphilis by the General Practitioner, J. Ven. Dis. Inform., (supp. 23) p. 1, 1949.

13. Davis, B.: Biologic False Positive Serologic Tests for Syphilis, Medicine, **23**: 359, 1944.

14. (*a*) Rein, C. R., and Elsberg, E. S.: Studies on the Incidence and Nature of False Positive Serologic Reactions for Syphilis, Am. J. Clin. Path. **14**: 461, 1944. (*b*) Rein, C. R., and Kostant, G. H.: Nature of Antigens and Antibodies in Serology of Syphilis, Arch. Dermat. & Syph. **60**: 217, 1949.

15. Stokes, J. H., and James, G. W.: The Problem of the "Biologic False" or Nonspecific Positive Serologic Test for Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **33**: 114, 1949.

16. Moore, J. E. and Mohr, C. F.: Chronic Biologic False Positive Reactions in Serologic Tests for Syphilis, to be published.

western states), at least half of seropositive reactors discovered in mass blood testing programs do not have syphilis at all, but do instead have biologically false positive reactions.

TWO TYPES OF BIOLOGICALLY FALSE POSITIVE REACTIONS

Increasing knowledge of the biologically false positive phenomenon has permitted its differentiation into two types, which for lack of better names may be designated as "acute" and "chronic."

TABLE 2.—*"Acute" and "Chronic" Biologically False Positive Reactions* *

Identified Causes, Laboratory Procedures, and Other Features	"Acute" †	"Chronic" ‡
Previous seronegativity	+	+ or 0
Exposure (history)	0	0
Exposure (epidemiology)	0	0
Verified episode precipitating cause	+	usually 0
Seropositivity during or after precipitating episode	+	usually 0
Physical examination for syphilis	0	0
Serologic titer (standard)	usually low	variable
Cerebrospinal fluid	not necessary	0
Spontaneous seroreversal	+	0
Treatment for syphilis	0	+ or 0
Duration seropositivity	3-6 months	months-years

* The zero indicates that negative information was obtained; the plus sign indicates that the factor is present or that positive results of tests are usually obtained.

† "Acute" reactions are usually associated with a bacterial, viral, plasmodial, or Rickettsial infection.

‡ "Chronic" reactions may be associated with an infection, usually leprosy, or a collagen disease.

Acute Reaction.—Acute biologically false positive reactions are characterized by the fact that they occur during or shortly after a wide variety of unrelated nonsyphilitic infections or conditions, and that they disappear spontaneously within a few days, weeks, or months (not more than six months) after recovery. Their causes and approximate incidence in the several disease processes are now fairly well known, and are summarized in table 1.

Chronic Reactions.—Chronic biologically false positive reactions are marked by the absence of the known precipitating factors listed in table 1, and by the fact that reagin persists in the blood over many months or years, perhaps even for a lifetime. So far, the only infectious disease known to produce chronic biologically false positive reactions in a high proportion of cases is leprosy, and this is not a large factor in their incidence, since leprosy is itself rare in this country and is moreover usually readily recognizable clinically. It is also clear that a proportion (not exactly defined) of patients with discoid or disseminated lupus erythematosus may show chronic biologically false positive reactions. Aside from this, knowledge as to their cause is still meager.

17. Scott, V.; Reynolds, F. W., and Mohr, C. F.: Biologic False Positive Spinal Fluid Wassermann Reactions Associated with Meningitis: Report of 8 Cases, Am. J. Syph., Gonor. & Ven. Dis. **28**: 431, 1944.

18. (*a*) Turner, T. B.: Protective Antibodies in the Serum of Syphilitic Rabbits, J. Exper. Med. **69**: 867, 1939. (*b*) Turner, T. B.; Fleming, W. L., and Brayton, N. L.: Protective Antibodies in the Serum of Human Syphilitics, J. Clin. Investigation **18**: 471, 1939.

19. Nelson, R. A., Jr.: Factors Affecting the Survival of Treponema Pallidum in Vitro, Am. J. Hyg. **48**: 120, 1948.

20. Nelson, R. A., Jr., and Mayer, M. M.: Immobilization of Treponema Pallidum in Vitro by Antibody Produced in Syphilitic Infection, J. Exper. Med. **89**: 369, 1949.

CLINICAL RECOGNITION OF BIOLOGICALLY FALSE POSITIVE REACTIONS

The clinical recognition of biologically false positive reactions is a time-consuming and laborious procedure, the details of which are summed up, both for acute and chronic reactions, in table 2. The symbol "O" in this table indicates that negative information was actually obtained. Thus, for any suspected biologically false positive reactor, epidemiological investigation (as a minimum, routine serologic testing) of familial and sexual contacts is essential, in order to verify the patient's statement of lack of exposure to the possibility of congenital or acquired syphilis. In all suspected chronic biologically false positive reactors, the spinal fluid must be demonstrated to be normal, since false positive serologic reactions in the spinal fluid do not occur (in contrast to blood serum) except in certain easily recognized neurological disorders (Scott, Reynolds, and Mohr [17]). Even with all these data in hand, clinical conclusions are far from accurate, as will presently appear.

SPECIFIC AND NONSPECIFIC ANTIBODIES IN SYPHILIS

The Treponemal Immobilization Test.—Turner (1939),[18] engaged in a study as to whether immunity in syphilis is cellular or humoral, first showed conclusively that the serum of syphilitic animals or man contained an antibody that combined directly with virulent T. pallidum. He incubated emulsions of the living organisms, derived from rabbit syphilomas, with syphilitic and normal serum; and, after an interval, inoculated the mixture intradermally in the skin of rabbits' backs. When normal serum was used, typical chancres appeared at the sites of inoculation after the usual incubation period, just as when the treponemes were suspended in isotonic sodium chloride solution. When syphilitic serums were employed, on the contrary, there was either no lesion at the portal of entry, or its appearance was greatly modified and the incubation period delayed. This phenomenon, indicating the presence in syphilitic serums of an antibody that destroyed T. pallidum organisms or at least interfered with their virulence, was not, however, utilizable in any practical manner.

TABLE 3.—*Results of Treponemal Immobilizing Test Compared with Clinical Judgment*

Clinical Diagnoses	Number of Cases	TPI * Test, % Positive	TPI * Test, % Negative
Syphilis, late, treated	262	256 (97.8)	6 (2.2)
Syphilis, latent, probable	167	142 (85.1)	25 (14.9)
Biologically false positive, probable	133	22 (16.1)	111 (83.9)

* TPI = treponemal immobilizing test.

Ten years later, working in Turner's laboratory, Nelson [19] undertook a study of the unsolved problem of growth of T. pallidum on artificial mediums. Although neither he nor others have as yet solved this problem, he was successful in maintaining the organisms alive, motile, and virulent for 5 to 10 days on an artificial medium largely free of tissue components. Having done this, Nelson and Mayer [20] evolved the simple idea of mixing an emulsion of motile treponemes in this medium with syphilitic or normal serum plus complement, and

observing the result directly under the microscope. When the mixture consisted of normal serum plus treponemes plus complement, nothing happened within 15 to 18 hours; the organisms remained motile and virulent. On the other hand, if syphilitic serums (from animals or man) were employed, the treponemes were immobilized and killed. By appropriate absorption experiments, it was next demonstrated that the antibody responsible for this phenomenon is distinct from reagin. Thus in syphilitic infection, at least two antibodies appear in the serum: (1) the nonspecific reagin and (2) a "treponemal immobilizing antibody."

Further studies, originated in the Johns Hopkins University [21] and promptly confirmed by other workers,[22] have provided much more information about the treponemal immobilizing antibody, as follows: 1. It does not occur in the serum of normal persons, or of those suffering from nontreponemal diseases. 2. It does occur uniformly in syphilis and the closely related treponematoses, yaws, pinta, and bejel, but not in other spirochetal diseases, such as leptospirosis, relapsing fever, rat-bite fever, or Vincent's infections. 3. In untreated syphilitic infection, its rate of appearance in the serum approximately parallels that of reagin; it is first detectable when the primary lesion is from 5 to 15 days old, and rapidly increases in titer for the first few weeks, reaching a plateau at about the second or third month of infection. However, in syphilitic rabbits, it does not decline or disappear from the serum following the spontaneous healing of the chancre, as does reagin; and it is probable (though not yet finally verified) that in man it does not spontaneously decrease in titer with the passage of years [23] (fig. 3).

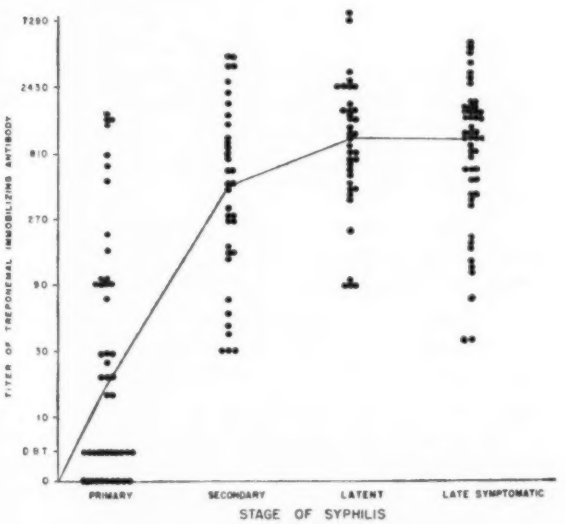

Fig. 3.—The titer of treponemal immobilizing antibody in untreated syphilitic infection in man (from Nelson [23]). The dots represent the individual observations of quantitative titer of treponemal immobilizing antibody in the serums of 158 humans with previously untreated syphilitic infection, and the curve indicates the median titer. The scale on the ordinate is logarithmic. Note that as with reagin (fig. 1), the titer rises rapidly during the first few weeks. Thereafter, however, and unlike reagin, it rises still further in subsequent years (the latent cases here are not limited to early latency, but represent for the most part patients with infections of many years' standing), and does not decrease with the passage of time.

In patients with untreated syphilitic infection, during and after the secondary stage, it is almost certainly always present for the duration of the patient's life even though reagin may have spontaneously disappeared; and the treponemal immobilizing test is therefore a useful diagnostic tool in reagin-free patients, i. e., those with negative standard serologic tests, with lesions possibly due to syphilis, such as in the differentiation between rheumatic and syphilitic aortic insufficiency. 4. In treated

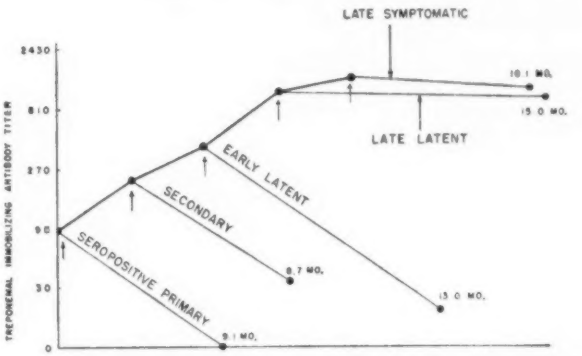

Fig. 4.—The behavior (within the first year) of treponemal immobilizing antibody in treated syphilitic infection in man (from Zellmann and Nelson [24]). These composite curves represent serial observations of the treponemal immobilizing test during the first 12 to 15 months after completion of treatment in five groups of patients, with seropositive primary, early secondary, early latent, late latent, and late symptomatic syphilis (the latter of various types). Note that the treponemal immobilizing antibody tends to disappear in persons with early syphilis, but at a somewhat slower rate than reagin. In those with late syphilis, however, whether it is latent or symptomatic, the titer remains unchanged in spite of treatment. In our own group of patients with late syphilis (table 3) whose treponemal immobilizing tests were usually done many years after the completion of treatment, quantitative data are not available, and would not be of much value if they were, since pretreatment observations for comparison are of course lacking. By extrapolation from the curves of figures 3 and 4, however, it is permissible to suggest that reduction in treponemal immobilizing titer probably does not occur in late syphilis (in contrast to reagin), regardless of the type or amount of treatment or the passage of time after its completion.

early (primary, secondary, or early latent) syphilis, treponemal immobilizing antibody disappears from the blood as does reagin, but at a slower rate and not necessarily in a parallel manner.[24] Thus, patients treated for early syphilis are usually found, years later, to be seronegative with both tests, though sometimes they are positive for treponemal immobilizing antibody and negative for reagin. 5. In treated late syphilis, i. e., of several years' duration, on the contrary, treponemal immobilizing antibody usually does not disappear from the serum, though reagin may do so (fig. 4); and such patients, examined from 1 to 35 years after clinically successful treatment of late syphilis of whatever type, are 95 to 98% positive to treponemal immobilizing antibody (table 3, fig. 4).

These and other data permit the tentative conclusion that the treponemal immobilizing test detects an antibody specific for syphilis and the related treponematoses, and

21. Nelson, R. A., Jr.; Zheutlin, H. E. C.; Diesendruck, J. A., and Austin, P. G., Jr.: Studies on Treponemal Immobilizing Antibodies in Syphilis: Incidence in Serum and Cerebrospinal Fluid in Human Beings and Absence in "Biologic False Positive" Reactors, Am. J. Syph., Gonor. & Ven. Dis. **34**: 101, 1950.

22. Magnuson, H. J., and Thompson, F. A., Jr.: Treponemal Immobilization Test of Normal and Syphilitic Serums, J. Ven. Dis. Inform. **30**: 309, 1949.

23. Nelson, R. A.; Zheutlin, H. E. C.; Austin, P. G. M., and Hill, J. H.: Applications of the Treponemal Immobilization Test to Problems of Clinical Syphilis, presented before the Symposium on the Latest Advances in the Study of the Venereal Diseases, Washington, D. C., April 27-28, 1950.

24. Zellmann, H. E., and Nelson, R. A.: The Effect of Penicillin Therapy on the Titer of Treponemal Immobilizing Antibody in Human Syphilitic Patients, presented before the Symposium on Recent Advances in the Study of Venereal Diseases, Washington, D. C, April 24-25, 1951.

that it may be expected, in a modified form, eventually to replace "standard" serologic tests that depend on lipoid antigens for detection of the nonspecific reagin. Unfortunately, this goal is not yet in sight, though efforts at simplification of the test are in progress and are promising. The treponemal immobilizing test is expensive, and since it is not yet possible to cultivate virulent T. pallidum in vitro, its performance depends on the maintenance of a large rabbit colony as a source of supply of living treponemes. It requires the use of sterile serum (or spinal fluid). It is time-consuming, complicated, and subject to numerous technical pitfalls. These difficulties have so far limited its use, largely on an experimental basis, to six or eight laboratories in this country, and it is not yet ready for adoption by the thousands of existing serologic laboratories.

APPLICABILITY OF TREPONEMAL IMMOBILIZING TEST TO RECOGNITION OF BIOLOGICALLY FALSE POSITIVITY

From the earliest development of the treponemal immobilizing test, it was obvious that its most practical and clinically important use might lie in the differentiation of the positive standard serologic test due on the one hand to syphilis and on the other to the biologically false positive phenomenon. This is in fact the case. Nelson and his associates [21] have demonstrated that the treponemal immobilizing test was negative in 12 acute biologically false positive reactors, in whom the false positive standard test was due to the following causes: primary atypical pneumonia in 6, infectious mononucleosis in 1, malaria in 1, chickenpox in 2, and measles in 2.

We,[25] on the other hand, have applied the test to the recognition of the much more frequent, difficult, and complicated problem of the chronic biologically false positive reactor. The validity of the test, under these circumstances, depends on the observation that in treated late syphilis, the treponemal immobilizing test remains positive, presumably for the duration of the patient's life, and in spite of the type or amount of previous treatment.

Our clinical material consists so far of 300 patients known to be seropositive with standard techniques for six months or longer (in some cases, as long as 10 to 15 years), and in whom the diagnosis lay between latent syphilis (no manifestations except the positive serologic test for syphilis) and the chronic biologically false positive phenomenon. Before the performance of the treponemal immobilizing test, our patients were assigned to one or other of these categories on the basis of the presence or absence of the collateral evidence outlined in table 2 (above).

The results of the treponemal immobilizing test in these two groups and in a group of 256 patients with clinically verified late syphilis, and the comparison of these results with clinical judgment, are shown in table 3. In the category of "syphilis, late, treated" the diagnosis in all cases depended on the presence of clinically recognizable lesions of the infection. In those classified as "probable latent syphilis" or "probable biologically false positive reactors," the clinical diagnosis depended on a verified positive standard serologic test for syphilis, plus, in each case, all or most of the collateral studies outlined in table 2.

From these data, it is suggested that there is a margin of error in both directions, which is probably of clinical judgment rather than of the treponemal immobilizing test, i. e., about 15% of patients in whom we had diagnosed latent syphilis were actually biologically false positive reactors; and 16% of those whom we had thought to be nonsyphilitic actually had syphilis. Nevertheless, the agreement between clinical diagnosis and the results of the treponemal immobilizing test is remarkably close.

INCIDENCE AND ETIOLOGY OF CHRONIC BIOLOGICALLY FALSE POSITIVE REACTIONS

Other than our own study and some as yet unpublished observations of Nelson [26] in the United States Navy, nothing is known so far of the incidence of chronic biologically false positive reactors. This information will not be forthcoming until larger scale serologic surveys have been undertaken in which all seropositive reactors with standard tests are checked by the treponemal immobilizing test. A guess may be made, however, that the phenomenon is frequent, since in our own practice, 43% of patients in whom in earlier years latent syphilis would have been diagnosed have now been identified as biologically false positive reactors (table 3).

Use of the treponemal immobilizing test permits, for the first time, a definite answer to the question, "Does this patient have syphilis?" When this question is answered in the negative, however, it is at once replaced by another and perhaps even more serious question: "What is the cause of the chronic biologically false positive phenomenon?" The answer to this latter question is not available from the existing literature. Surveys of the incidence of presumed biologically false positive reactions in this or that population group or in this or that nonsyphilitic morbid process are not valid, because positive standard tests with lipoid antigens have in no instance been checked by the treponemal immobilizing technique (except in the case of leprosy [27]).

The etiologic background of the chronic biologically false positive phenomenon is under study in this clinic, by means of a long term clinical follow-up of such patients. Only preliminary results are so far available, but these indicate that the biologically false positive reaction is not innocuous, to be dismissed lightly, but is often, perhaps usually, a manifestation of serious underlying disease. Outstanding among the conditions so far identified in a substantial proportion of biologically false positive reactors are the collagen diseases such as disseminated lupus erythematosus, periarteritis nodosa, rheumatoid arthritis, and rheumatic fever, and sarcoid. Further details of these studies will appear later.

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25. Mohr, C. F.; Moore, J. E.; Nelson, R. A., and Hill, J. H.: Studies on the Relationship of Treponemal Antibody to Probable Biologic False Positive Serologic Tests for Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **34**: 405, 1950.

26. Nelson, R. A.: Treponemal Immobilization Test Program in the U. S. Navy, presented before the Symposium on Recent Advances in the Study of Venereal Diseases, Washington, D. C., May 1-2, 1952.

27. Nelson has shown that 57 lepers seropositive by standard tests (76% of those tested), 46 were negative with the treponemal immobilizing test. The incidence of positive reactors with the latter test was about the expected incidence of syphilis in the racial and socioeconomic groups from which the lepers were drawn.

SUMMARY AND CONCLUSIONS

Standard serologic tests for syphilis are nonspecific, both as to antigen (an alcoholic lipoid extract of various normal animal or plant tissues) and antibody (reagin, which occurs not only in association with the treponematoses but also in various normal animal species, including man, and in man, in various nonsyphilitic infections and conditions). Confirmed (to exclude technical error) positive standard serologic tests occurring in the absence of treponemal infection are called biologically false positive reactions. The coincidence of mass blood testing and of World War II has provided much new information concerning them. Biologically false positive reactions are of two types: "acute" and "chronic." The former are associated with various infections, usually acute, the most important of which are listed. The etiologic background of chronic biologically false positive reactions is not as yet clear.

The serum of syphilitic animals or man contains, in addition to reagin, another antibody distinct from reagin, called the treponemal immobilizing antibody. This antibody is not present in normal persons or in those with nonsyphilitic diseases. A test for its recognition (treponemal immobilizing test) may be used for the differentiation of the "true" positive reactions in syphilis and biologically false positive reactions. The behavior, both reagin and treponemal immobilizing antibody during the spontaneous evolution of syphilitic infection and as affected by antisyphilitic treatment, is described.

Among certain groups of persons having no history or physical evidence of syphilis but found routinely to be seropositive with standard techniques, nearly one-half do not have syphilis, but are biologically false positive reactors. Chronic biologically false positive reactions are usually a manifestation of serious underlying disease, sometimes of the group of collagen diseases. Every effort should be made to distinguish between syphilis and the biologically false positive reaction, and if the latter is identified, the patient should be carefully examined and followed in order to determine its cause.

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THE PATIENT WITH UPPER GASTROINTESTINAL TRACT HEMORRHAGE

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To the patient, relatives, and physician alike, the presence of gastric hemorrhage creates an alarming situation, fraught with a sense of emergency and the impelling feeling that something should be done immediately. It is on the attending physician that the burden of responsibility rests. It is of primary importance for him to assume his role in a confident manner, reassure those concerned, and allay the anxiety of the bleeding patient. This may properly be done by an honest, sincere explanation in terms the latter can understand and appreciate, without minimizing the seriousness of the condition. At the same time the physician must formulate for himself a plan of management that is appropriately proportional to the severity and rate of the bleeding, age of the patient, and history of antecedent gastrointestinal trouble.

Successful management is based on accurate and early diagnosis. The general practitioner to whom the average patient generally appeals for help is charged with this responsibility. To obtain this effectively, an understanding of the problem is of primary importance. The following facts should be considered. The causes of hemorrhage from the gastrointestinal tract are variable. It is worthy to note that 75% of all intestinal tract bleeding and 90% of intragastric bleeding, which present hematemesis and melena, are due to peptic ulcer,[1] and of such patients about 16% have no history of previous ulcer symptoms.[2] Such is demonstrated in the following case.

CASE 1.—In March, 1951, a 45-year-old business man without previous gastrointestinal symptoms felt faint, slightly nauseated, and thirsty. After drinking a glass of water he vomited a large panful of dark brown blood. Hematemesis and melena continued for the next six days in diminishing proportions. Careful elicitation of history failed to give any indications of an ulcer. At no time was there any pain. X-ray examination showed a definite duodenal ulcer.

As one would readily suspect, hematemesis generally results from a gastric ulcer and presents more active, but not necessarily more dangerous, bleeding. Duodenal ulcer produces a slower, oozing variety of bleeding; however, any lesion of the gastrointestinal tract, including the rectum, will be tarry if it is not passed for several days.[3] Typical is the following case, which is reported in order to emphasize the danger of slow, progressive, insidious oozing with weakness and fainting, commonly following the passage of a large tarry stool.

CASE 2.—On March 15, 1947, at about 3 a. m., a business man, aged 64, was found in a semicoma lying on the bathroom floor of his home in a pool of vomited blood. Two days previously, he recalled later, he had become nauseated and had fainted after passing a large tarry stool. He denied any recent gastric pain or distress. A local physician was called, and morphine was given subcutaneously; the patient's diet was restricted in fluids and food, and he was kept in bed. During the day he had a large, coffee-ground vomitus, and in the evening of the following day he was referred to the hospital. In 1934, he recalled later, he had been placed on an ulcer regimen for four months, after a roentgen ray examination during the course of investigation for epigastric distress. Except for hyperactive reflexes and tarry residue in the rectum, the thorough examination showed that urine was normal, hemoglobin was 9.4 gm. (Sahli method), red blood cell count was 3,050,000, and white blood cell count was 6,000, with 75% segmented cells.

Because of the relatively good condition of the patient at this time it was felt that conservatism was the course to follow, and he was placed on a modified Andresen regimen, consisting of hourly feedings of skimmed milk and gelatin solution, with hard candy between feedings. Meperidine hydrochloride and barbiturates were administered freely for restlessness and pain. During

1. Bockus, H. L.: Gastro-Enterology, Philadelphia, W. B. Saunders Company, 1943, vol. 1, p. 560.
2. Ivy, A. C.; Grossman, M. I., and Bachrach, W. A.: Peptic Ulcer, Philadelphia, The Blakiston Company, 1950, pp. 806, 809.
3. Lindenmuth, W. W.: Symposium on Surgical Diagnosis: Hemorrhage from Gastrointestinal Tract, S. Clin. North America 30: 1613, 1950.

the afternoon of the following day he became extremely faint, vomited a large amount of bright red blood, and chilled; the pulse became rapid and irregular as he showed signs of air hunger and hemorrhage. The hemoglobin dropped to 6.3 gm., the red blood cell count dropped to 2,650,000, and the white blood cell count rose to 10,000. In spite of sedation, blood transfusions, and administration of vitamin K, liver extract, epinephrine orally, and dextrose and isotonic solution of sodium chloride with human blood plasma subcutaneously, his condition became more precarious with each succeeding day. On March 20, 1947, the red blood cell count dropped to 1,800,000 and the temperature rose to 103.6 F, the pulse rate to 140, and the respiration rate to 40. He was irrational, confused, noisy, and uncooperative. Each transfusion appeared to initiate bright red vomitus and large involuntary tarry stools.

Most fatalities occur because the hemorrhage persists or recurs. Very few are rapid in onset and immediately fatal; therefore, time is allowed to modify one's original plans to what seems best with the case at hand. Persistent hemorrhage is about 10 times more likely to cause death than recurrent hemorrhage.[4] Persistent melena in itself is not an unfavorable sign, but when it is followed by bright red blood with repeated stools dangerous bleeding is persisting. This indicates that the vessel is being held open by adjacent induration of previously scarred tissue and is not allowed to constrict and clot.[5] In these cases previous ulcer history is the rule, and at postmortem or postoperative examination stiff indurated vessels are found at the base of a chronic ulcer. Most large hemorrhages from ulcers are duodenal, and only a minority are due to erosions into the large adjacent vessels, such as the often blamed pancreaticoduodenal, gastroduodenal, and pyloric arteries. Most bleeding originates from small, actively congested areas surrounding the ulcer base or from vascular buds in the crater. After a considerable hemorrhage it is frequently observed that the ulcer heals rapidly and the patient is asymptomatic in a short time.

Because accurate diagnosis is necessary it is appropriate to notice other causes of bleeding and to point out that during this early period it is safe to apply the general principles of treating the hemorrhage that are to be laid down subsequently. At the same time appropriate differential tests may be applied. Schindler [6] has emphasized the importance of erosions due to gastritis and duodenitis as a cause of fatal hemorrhages. Malignancy should be ruled out. When bleeding is the first and only sign, benign tumors such as liomas, diverticula, polyps, and neurofibromas make themselves known often by massive hemorrhage. Hiatus hernia bleeding is rarely massive.[3] Hampton [7] has demonstrated that early careful roentgenography of the upper gastrointestinal tract may be safely done to establish diagnosis. Cirrhosis of the liver causing varicose esophageal veins and congestion of the stomach is seldom the cause of massive hemorrhage and in itself is rarely fatal. Warren Cole [8] emphasizes the fact that the two most common causes of hematemesis are peptic ulcer and esophageal varices. The bromsulfalein test and increase of urobilinogin in the urine are the most valuable tests in the latter condition. Splenic anemia, Banti's syndrome, polycythemia, and purpura with diseases and tumors of the gallbladder, pancreas, small intestine, and appendix are of relatively diminishing importance in a list of etiological factors. For the sake of completeness one should add cardiac failure, epistaxis, swallowed blood, malingering, and vicarious menstruation.

Shock is among the first signs noted in the loss of large amounts of blood, and the signs and symptoms of circulatory failure are apparent: i. e., chilliness, weakness, slight nausea, and syncope with defecation. During the first 24 hours, often there is a temperature that may range up to 103 F, and this may last for a few days. Because the body is responding to the threatened exsanguination, there is initial constriction of the blood vessels with a secondary pressure rise. The pulse and blood pressure readings are not too reliable unless taken every hour or so; but they cannot be totally disregarded when the pressure drops to below 90 and the pulse is over 120, for then the prognosis is exceedingly grave. Likewise, hemoglobin and blood counts are only of relative value. In other words, they are only adjuncts to prognosis. They have a place, but alone they are not too reliable. Theoretically blood volume determinations should be ideal, but they are too complicated to be practical and are of little clinical value.[9] Schiff [10] showed the value of prerenal azotemia, and this test should be briefly discussed at this time for it is the one test of prognostic value. The blood urea nitrogen rises from its normal of between 10 and 15 to 100 mg. per 100 cc. or more the first day of the hemorrhage, and if there is no more bleeding it returns to normal after 48 hours. Its elevation is proportional to the number of hemorrhages and the amount of blood loss. After recession an elevation of the blood urea level indicates repeated bleeding and carries with it a proportionally grave prognosis; conversely a rapid fall is a favorable sign. Hyperazotemia is an expression of the amount of blood protein absorbed from the bowel.[11] Albuminuria does not occur as a result of hematuria. Progressive diminution of the urinary amount is also a bad prognostic sign if the fluid balance is maintained. In discussing the laboratory phase I do not wish to give the impression that coagulation time, bleeding time, platelet count, and prothrombin time are not of value. They should be done as a means of etiological differentiation.

The older the patient the higher the incidence of morbidity and mortality. As Blackford [12] pointed out in his review of Seattle's vital statistics, 96% of the hemorrhagic deaths from peptic ulcer occur after the age of 45. History of antecedent gastrointestinal symptoms shows an increase of mortality of about three times that of an

4. Andresen, A. F. R.: Management of Bleeding Peptic Ulcer, in Management of Common Gastro-Intestinal Diseases, The American Practitioner Series, edited by T. A. Johnson, Philadelphia, J. B. Lippincott Company, 1948, p. 48.

5. Chinn, A. B., and Wickesser, E. C.: Acute Hemorrhage from Peptic Ulceration: An Analysis of 322 Cases, Ann. Int. Med. **34**: 339, 1951.

6. Schindler, R.: Gastroscopy: The Endoscopic Study of Gastric Pathology, Chicago, University of Chicago Press, 1937, p. 343.

7. Hampton, A. O.: Safe Method for Roentgen Demonstration of Bleeding Duodenal Ulcers, Am. J. Roentgenol. **38**: 565, 1937.

8. Cole, W. H.: Symposium on Gastroesophageal Surgery: Surgical Treatment of Bleeding Peptic Ulcers, S. Clin. North America **31**: 271, 1951.

9. Ivy, Grossman, and Bachrach,[3] p. 807.

10. Schiff, L., and Stevens, R. J.: Elevation of Urea Nitrogen Content of Blood Following Hematemesis or Melena, Arch. Int. Med. **64**: 1239, 1939.

11. Bockus,[1] p. 586.

12. Blackford, J. M., and Cole, W. S.: Massive Hemorrhage from Peptic Ulcer: Study Based on Vital Statistics of City of Seattle During 4 Years and on Personal Experiences in Private Practice, Am. J. Digest. Dis. **6**: 637, 1939.

uncomplicated case.[1] These facts are well substantiated by others. All in all, it must be remembered that individualization in each case is essential not only to the prognosis but also to the subsequent management. With this in mind, the physician can best treat his patient successfully. Critical evaluation, reassurance, and proper selection of sedation are the prime requisites for successful management of the bleeding patient. Any attempt to obtain a clear-cut plan of management by reviewing the current literature today appears to be conflicting and confusing. Some internists, following the teachings of Meulengracht [13] and Andresen,[4] state that as long as 98% of the patients recover under medical management there is no need to resort to surgery. Finsterer [14] and his group point to their 5 to 6% mortality and state that the medical men are including in their group superficial ulcerations with slight bleeding, which would stop without hemostatic therapy. Recently Brown and Meyers [15] reported a mortality of 87% in cases of massive hemorrhage from peptic ulcer treated medically as compared to 12.5% in cases treated surgically at Detroit Receiving Hospital. The most important single influence on the death rate is bleeding after hospital admission. Both sides present convincing arguments and impressive statistics. Certainly there must be some midpoint of agreement that is applicable and that can be determined only when the patient is individualized, the thought kept in mind that he is the most important factor and his complete recovery is our goal.

Shock, when it appears as a result of massive hemorrhage, must be combated first by bedrest, sedatives, barbiturates, and/or chloral hydrate. The Trendelenburg position is not recommended, for there is evidence to show that it not only does little good but may be harmful and will increase the depth of shock, so the bed should remain flat. The patient should be kept warm but additional covers and external heat need not be applied, for the resultant superficial dilation of blood vessels does not help the patient's decreased blood volume. Morphine is mentioned here to condemn its use, in spite of its extensive employment in the past, for these reasons. 1. Pain here is not a problem, as the blood in the stomach relieves the ulcer pain.[8] 2. Restlessness and anxiety are the factors to combat. 3. Individual sensitization, respiratory depression, tendency toward duodenal spasm, and nausea with vomiting, along with its general unpredictable reaction, make morphine an unreliable drug and should preclude its use. 4. In shock we already have a low circulating blood volume, poor cardiac output, arterial vasoconstriction, slow capillary flow, and reduced peripheral constriction; if morphine is given subcutaneously under these circumstances, it is slowly absorbed, if at all, and when it does act it further depresses the blood pressure, antagonizes vasoconstriction, lowers the blood volume, and further depresses cardiac output.[16] In other words, contrary to former teachings, morphine deepens shock and does not combat it. Ephedrine-like compounds and intravenously administered glucoses have been shown to do more harm than good, for the restlessness, excitement, and apprehension that are manifest with hemorrhage are increased in shock. To tone down these symptoms chloral hydrate or paraldehyde by rectum or phenobarbital (luminal®) sodium intramuscularly are useful. I have had particularly good results with the addition of 10% thiopental (pentothal®) sodium into the blood transfusion tube in acute cases where rapid sedation is desired; it also has long-lasting effects, and it may safely be repeated as necessary.

Adequate and rapid replacement of blood is without equal in the treatment of shock due to hemorrhage. Plasma and the newer blood substitutes have their places as secondary choices while blood is made available. The blood should be rapidly administered through a 15 or 18 gage needle intravenously or intra-arterially as recently demonstrated by White and Stubb in utilization of the radial artery.[17] It seems that the former idea that increasing blood volume in this way will increase hemorrhage has been sufficiently disproved to preclude further discussion. It must be remembered that bleeding patients die of anoxemia and the longer the anoxemia exists the greater the danger. There is no substitute for hemoglobin to correct the anoxemia.[18] Seldom does one err in giving too much blood. It must be given adequately and rapidly. Too often we abide by our Anglo-American tradition: "Too little and too late."

In securing blood for transfusion the question of the Rh-negative patient is a stumbling block, particularly in small hospitals where blood banks are not feasible. In this regard, Dr. John R. Paine [19] has offered this helpful note. "[We found it to be true in practice] that if you have an Rh negative patient who has never been transfused before, you can give that patient all the Rh positive blood that you wish for 72 hours, but after that period of time you run a very grave risk, and the risk is more grave with each transfusion." The patient, not the pulse nor the blood pressure only, is the determining factor in the improvement.

After shock has been successfully combated the next step is to stop the bleeding. As elsewhere in the body, nature has a tendency to promote healing and prevent further destruction in the ulcerated area unless some mechanical difficulty ensues, such as is found with indurated scar tissue holding open a bleeding vessel. Ordinarily, however, when bleeding occurs the body mobilizes all factors to aid coagulation. The prothrombin level is raised, blood pressure is lowered, and the vessels constrict. Utilization of these facts has aided materially in the successful results obtained in the thrombin treatment of intragastric hemorrhage. It is the slow, long-continuing or frequent, intermittent bleeding that is

13. Meulengracht, E.: Fifteen Years' Experience with Free Feeding of Patients with Bleeding Peptic Ulcer: Fatal Cases, Arch. Int. Med. **80**: 697, 1947.

14. Finsterer, H.: Surgical Treatment of Acute Profuse Gastric Hemorrhages, Surg., Gynec. & Obst. **69**: 291, 1939.

15. Brown and Meyers, cited by Johnston, C. G.: Hemorrhage from the Upper Gastrointestinal Tract, editorial, Surg., Gynec. & Obst. **91**: 759, 1950.

16. Jeghers, H., and Brick, I. B.: Hazards in the Therapeutic Use of Morphine, M. Clin. North America **34**: 1761, 1950.

17. White, C. S.: Paper read at Sixteenth Annual Assembly, International College of Surgeons, Sept. 10, 1951.

18. Stewart, J. D.; Rudman, I.; Citret, C., and Hale, H. W., Jr.: Definite Treatment of Bleeding Peptic Ulcer, Ann. Surg. **132**: 681, 1950.

19. Paine, J. R., in discussion on Glenn, F.: Secondary Operations for Peptic Ulcer, Ann. Surg. **132**: 714, 1950.

dangerous to life. Thus, the longer the bleeding the more serious the problem. Any aid in controlling or stopping this insidious bleeding is of value. I first used thrombin to combat massive hemorrhage in March, 1947, and reported the case in THE JOURNAL the following July.[20] Since that time I have had the opportunity to use it successfully on other patients. Also, there has developed a keen personal interest in the problem of management of intragastric bleeding. Current literature references have condemned thrombin therapy as being useless or of little value and only rarely has it received much praise. It has, however, been used by others with success, particularly Daly, Johnston, and Penberthy[21] who succeeded in 87% of unselected cases with only one death.[15] I believe it is a definite adjunct to treatment and has its place in controlling the dangerously slow oozing blood vessel and in the saving of lives. The method of administration is simple but effective: have the patient drink or slowly sip 1 oz. of the freshly prepared buffered solution every two hours between bland feedings. I find no reason for combining it with gelfoam® (absorbable gelatin sponge) as is advocated by Cantor, Kennedy, and Reynolds.[22] I do not think it wise to introduce a stomach tube while active bleeding is present. Immediately following hemorrhage, digestion of the clot or vessel by strong gastric juice is satisfactorily prevented by the digestion of the free blood in the stomach, which in turn neutralizes the acid.[23] By the addition of thrombin, the clotting mechanism, retraction, and healing have been accelerated so that subsequently formed gastric juice will not be so apt to attack the organized clot. The buffered solution further aids in neutralizing the gastric juice; so with the neutralized blood, thrombin may act more quickly. If bleeding is so active that thrombin cannot reach the bleeding point, it cannot be expected to stop the hemorrhage; therefore, we know we are dealing with one of the rarer large vessel erosions with rapid exsanguination. Again the reaction of the patient and the stoppage of the bleeding are the important matters at the moment. As Andresen[4] and others[24] have noted, patients who are immediately and often fed after hemorrhage did better than those on the starvation treatment. For one thing excessive acid juices also are neutralized by the ingested food. Alvarez[25] and Ivy[26] have shown that a full stomach with slow even peristalsis is more at rest than an empty one with tonic irregular contractions, which may disturb the organized clot.

The introduction of ice or icy drinks only congests the gastric mucous membrane and invites further bleeding. I do believe that those who favor bland, palatable frequent feedings are correct. The following is the feeding schedule I have recently used in active bleeding: This mixture is mixed by the use of an ordinary eggbeater.

"Lipomul" orally, which contains 40% emulsified vegetable oil and 10% dextrose	2 oz.
Milk	8 oz.
Somagen,® solubilized (a mixture of milk proteins and yeast and liver concentrates), which contains 70% protein by weight	1 tbs.
Corn syrup, which may be flavored with vanilla or chocolate if desired	2 oz.

This feeding is given orally every two hours, alternating with the buffered thrombin solution, proportional to the amount and duration of the gastric bleeding. As rapidly as is tolerated, the following foods are added at regular meal times: farina, soft cooked egg, butter, melba toast, cream, sugar, potato, soup, malted milk, custard, and chocolate pudding. Here again the patient's response is the index to the quantity of food accepted. The orally administered "lipomul" is continued bihourly until bleeding has ceased.

While formerly the gelatin, fruit juice, and gruel feedings, as advocated by Andresen, were used with success, this feeding was substituted because it adequately furnishes calories and protein requirements in a small quantity of feedings. Too often unpalatable and increased quantities of food overtax the patient, discourage eating, and add to anorexia, as is often found in patients who are given cream and milk mixtures. In addition to the suggested feeding vitamin B complex and vitamin C are given parenterally. The solution is also given by tube on the second, third, and fourth postoperative days following gastric surgery. This treatment is a modification of that devised by Andresen in 1916.

What should be done about the patient who does not do well on conservative management? First of all, his status must be carefully reevaluated from time to time. The procedures should be modified to suit the occasion. In general, I believe that every patient is entitled to a fair chance at conservative treatment. Recurrent shock, recurring hyperazotemia, and gross manifestations of massive hemorrhage not responding to a fair chance on thrombin and frequent feedings is indication for surgical intervention. I do not mean that surgery is to be used as the last resort; surgery is a supplement, when indicated, to medical management. Every surgeon will use most of the methods outlined to get his patients in the best preoperative condition possible. Time is not lost by combating shock, correcting dehydration, and providing for and giving adequate blood. Administering thrombin and feeding the patient according to this plan does not interfere with necessary preoperative preparation. By the time this is done the problem of surgical intervention can be decided upon.

Experience in World War II has shown us that a healthy person can stand acute blood loss much better than long-continued or intermittent bleeding.[19] Also, there is a trend now toward more radical procedures, such as gastric resection including the ulcerated area. With adequate anesthesia, plenty of blood, and sufficient help, these patients stand this operation surprisingly well. Like medical treatment, figures on the mortality of the surgical patients have definitely improved in recent years.

20. Rogers, T. M.: Management of Gastric Hemorrhage Using Topical Thrombin, J. A. M. A. **137**: 1035 (July 17) 1948.

21. Daly, B. M.; Johnston, C. G., and Penberthy, G. C.: The Management of Patients with Bleeding from the Upper Gastro-Intestinal Tract with Buffer and Thrombin Solution, Ann. Surg. **129**: 832, 1949.

22. Cantor, M. O.; Kennedy, C. S., and Reynolds, R. P.: Gelfoam® and Thrombin in Treatment of Massive Gastrointestinal Hemorrhage, Am. J. Surg. **82**: 230, 1951.

23. Alvarez, W. C.: Introduction to Gastro-Enterology, ed. 4, New York, Paul B. Hoeber, Inc., 1948, p. 445.

24. Alvarez,[23] p. 455.

25. Alvarez,[23] p. 467.

26. Ivy, A. C.: Contributions to Physiology of Stomach: Causes of Gastric Secretion: Their Practical Significance and Mechanisms Concerned, J. A. M. A. **85**: 877 (Sept. 19) 1925.

Another important point of consideration, which faces every general practitioner to whom the majority of this type of patient turns and which has much to do with the determination of the subsequent procedures, is what is currently available. There is not always a physician present whose surgical experience coincides with the demands of the case at hand. Medical management thoroughly and adequately employed is certainly superior to surgical intervention when it is only halfway adequate. In general, simple ligation of a bleeding vessel is not such a simple untraumatic experience as its connotation might imply, for in a relatively inaccessible bleeding area it is often difficult to locate the site and extent of the bleeder.

What about the patients, and these are in the majority, who have stopped bleeding? In about two weeks, complete x-ray examination can be performed without risk. Diagnosis is established; now, surgery, if it is considered advisable, is elective. There is no question regarding the benign or malignant tumor unless it be one of the extent of metastasis. The patient with the nonobstructive ulcer who has recovered from an hemorrhagic episode should have the causative factor removed if it is at all practical. In the first place, as Ivy [2] pointed out, 66% will bleed after continued medical management, 23% after gastroenterostomy, and 11% after gastric resection. Of those under medical management 20% will remain difficult to handle and will experience recurrent severe hemorrhage. Secondly, the type of persons who have peptic ulcers are generally tense and anxious, and their disturbed processes of digestion accompany emotional upheavals, reacting adversely to emotional states and turmoil. Experience with one hemorrhagic attack leaves a definite memory of the accompanying fears and insecurity, which in turn has reason to bring back tension-anxiety states. What reassurance can the physicians give this patient regarding a recurrence of bleeding? I think it important to consider the patient's feelings and at the conclusion of medical therapy operate before opportunity is allowed for the recurrence of hemorrhage. Provided there is no serious intercurrent bleeding, that time is ideally about two to three months later.[27] Surgery promises fewer recurrences and a greater chance of becoming symptom free. In evaluating a difficult case we must weigh the evidence of a somewhat higher mortality and decreased morbidity offered by surgery against the chances of prolonged and repeated episodes of hemorrhage and pain of the medical regimen.

It has been amply demonstrated that the formerly popular simple gastroenterostomy in the absence of obstruction will often relieve pain but is not sufficient protection against further hemorrhage. There is, however, some indication that this procedure, with vagotomy, has a place in the elderly and severely debilitated patient; (Sawyer,[28] Dragstedt,[29] Meyer [30]); however, it is too early to adequately evaluate the results. This procedure accomplishes good results in the complicated anastomotic ulcer with hemorrhage as compared with gastric resection, following which Marshall [31] reports success in 2.4% of cases. Except for this, all in all, subtotal gastric resection is the operation that has stood the test of time.[32] On the basis of my limited experience, I prefer the modified Hofmeister technique of the Polya operation, consisting of placement of the gastrojejunal anastomosis at the greater curvature, removing two-thirds to three-fourths of the stomach, and including, if at all possible, the ulcerated area. At present there is not a meeting of minds among surgeons regarding the desirability of totally removing the complicated ulcer of the duodenum.[33] Recurrent bleeding of the old ulcer bed that is not removed is rare. The mortality of gastric resection is due more to complications arising from faulty duodenal closure than from the operation itself.[34] The method of implanting a catheter into the distal stump, as advocated by Priestley and Butler [35] at the Mayo Clinic, may do much to overcome these pitfalls, as I have just recently experienced.

A final word regarding postoperative care is appropriate here. It is surprising how readily the patient who has undergone a gastrectomy recovers from this major procedure and how quickly he gains back his former well-being except for the occurrence of a macrocytic type of anemia, which does not respond well to liver but does respond to folic acid and vitamin B_{12}, whether administered orally or parenterally. Follow-up blood cell counts are as important as are follow-up x-ray examinations. The possible complications of surgery are, in order: dumping syndrome, recurrent ulceration, recurrent bleeding, and severe atony.

SUMMARY

The purpose of this paper is to discuss concisely from the standpoint of the general practitioner a method of proper management of the patient who is bleeding from the upper gastrointestinal tract, with emphasis on gastric hemorrhage due to peptic ulcer.

The following points are stressed: (1) treatment of the individual patient according to his changing condition, (2) early and accurate diagnosis, (3) danger of slowly progressive and recurrent bleeding, (4) avoidance of morphine and use of proper sedation in the treatment of shock and hemorrhage, (5) value of introducing large amounts of blood rapidly, (6) efficiency of utilizing the physiological response to frequent palpable feedings, and (7) role of orally administered buffered thrombin solution and the role of surgery in treatment of the patient with gastric hemorrhage.

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28. Sawyer, K. C.: Personal Evaluation of Vagotomy in Treatment of Peptic Ulcer, J. Internat. Coll. Surgeons **15**: 585, 1951.

29. Dragstedt, L. R.: Paper read at Sixteenth Annual Assembly, International College of Surgeons, Sept. 10, 1951.

30. Meyer, K. A., and Stein, I. F., Jr.: Recurrent Peptic Ulcer Following Surgical Intervention: Diagnostic and Therapeutic Problems, J. Internat. Coll. Surgeons **15**: 725, 1951.

31. Marshall, S. F.: Partial Gastric Resection for Peptic Ulcer, S. Clin. North America **29**: 767, 1949.

32. (*a*) Bancroft, F. W.: Surgical Problems of Duodenal Ulcer, J. A. M. A. **147**: 364 (Sept. 29) 1951. (*b*) Healy, M. J., Jr.; Hellman, S. J., and Sauer, P. K.: Vagotomy Versus Gastric Resection: Comparative Evaluation of Relative Effectiveness in a Controlled Series of Cases, ibid. **147**: 368 (Sept. 29) 1951.

33. Bancroft.[32a] Welch, C. E.: Surgery of Stomach and Duodenum: A Handbook of Operative Surgery, Chicago, The Year Book Publishers, Inc., 1951, pp. 49-52.

34. Marshall.[31] Bancroft.[32a]

35. Priestley, J. T., and Butler, D. B.: Duodenostomy: Method of Managing Duodenal Stump in Certain Cases of Partial Gastrectomy, Proc. Staff Meet., Mayo Clin. **26**: 65, 1951.

CLINICAL NOTES

POSTMORTEM OBSERVATIONS TWENTY YEARS AFTER BILATERAL MASTECTOMY

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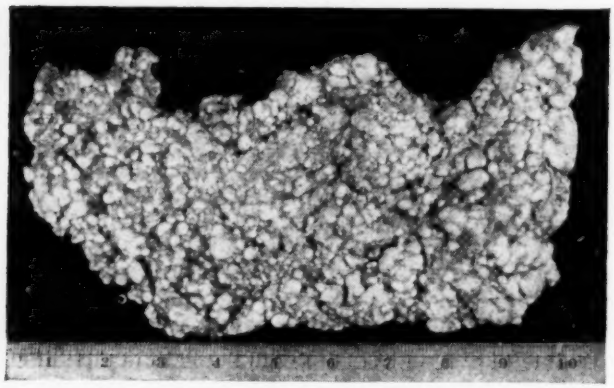
A recent excellent article on the treatment of breast cancer has encouraged the presentation of this report. The case in question is one in which autopsy was performed by me in 1941. Prior to the presentation of the details of this case, mention will be made of several facts noted in the article previously mentioned.[1]

There is some confusion about the best methods of treatment for cancer of the breast. Authors present statistics showing the survival rate of patients five years after operation. The cases usually are grouped into those in which radiation therapy was given either before or after mastectomy (or both) and those in which surgery alone (either simple or radical mastectomy) was performed. In the article mentioned above, the authors discuss a patient



The omentum in the case reported, showing metastatic nodules.

with advanced cancer who was subjected to surgery and was well 14 years after mastectomy (no mention is made of radiation therapy). These authors mention other cases in the literature. Since the acceptance of hormonal therapy as a postoperative regimen, this knowledge is also included in reports referring to similar long survivals. However, few have been recorded beyond the 14-year period. These authors are of the firm belief that their case (and others in the literature) is evidence of tissue resistance to cancer growth. They "thank tissue resistance for saving this patient. The facts indicate that this can hold cancer in check for many years. It probably accounts for our favorable results following axillary dissections for cancer."[1]

This quotation on tissue resistance to cancer is an extremely important observation. My own thought has been that there is some immunity or pseudoimmunity to cancer. It may be called by any name. No matter what the term, many clinicians have observed that, given two patients with the same type of cancer, of approximately the same age with the same duration of the disease, one patient may die within a year and the other may survive for many years. Other observations demonstrate that certain families have a low resistance to cancer. This disease may cause the death of several members of the family before the fifth decade of life. Members of other families live to advanced ages of 80 and 90 with no history of cancer in any member. Death results from the infirmities of old age.

The following report of a case is a point in favor of the theory of tissue resistance, or pseudoimmunity, to cancer.

REPORT OF A CASE

Mrs. E. H., aged 60, had a bilateral mastectomy in Germany 20 years prior to her death. She did not receive any postoperative therapy.

After her operation she had no unusual illnesses and continued to work in her normal routine. She came to America 10 years after the operation and carried on her family duties. She had four children, all born prior to her operation. Her health failed six months before her death. The complaints were progressive loss of weight and a nonproductive cough. One month before her hospitalization and death, ascites developed. Abdominal paracentesis was performed by her family physician on several occasions. When the ascites recurred rapidly after paracentesis (within two or three days), hospitalization was advised.

The patient died shortly after admission. (No familial history of cancer was obtained from the children.)

An autopsy was performed, which demonstrated carcinomatosis. Cancer nodules were found from head to knees and to both elbows. No metastases were found in the extremities beyond the elbows or the knees. The skeleton and the viscera were studded with adenocarcinoma. An idea of the diffuse process can be obtained by the accompanying photograph of the omentum, which was completely invaded with cancer nodules resembling countless pearls of varying sizes.

COMMENT

The postmortem observations in this patient, who had cancer for 20 years, are explainable on the basis that "tissue resistance," or pseudoimmunity, allowed only the slow progression of the disease until a period was reached when the pathological process overcame the resistance. At this point death was inevitable. The absence of metastases beyond the elbows and knees can be explained according to the investigations of Batson.[2] He demonstrated the existence of a system of vertebral veins extending from the coccyx to the skull that communicate with the veins in the ribs, shoulder girdle, pelvic girdle, upper end of the humerus, and femur.

This case illustrates the possible presence in some persons of a resistance to cancer. Although the disease is present, its growth is inhibited and its spread retarded. In this case the lesion was the usual variety of adenocarcinoma of the breast. Both breasts were amputated, because tumor masses were found bilaterally. Whether cancer was present in both breasts could not be determined from the history.

The question of immunity to diseases other than cancer is well known and accepted. Although no definite proof can be advanced for the existence of a pseudoimmunity, or tissue resistance, to cancer, nevertheless, clinical experience and observation lend credence to the possibility that it may exist.

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2. Batson, O. V.: Function of the Vertebral Veins and Their Role in the Spread of Metastases, Ann. Surg. **112**: 138 (July) 1940.

SUMMARY

A case of a 20-year survival following bilateral mastectomy for adenocarcinoma is reported. The question is raised concerning the possibility of tissue resistance, or pseudoimmunity, to cancer.

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PAROXYSMAL VENTRICULAR TACHYCARDIA DUE TO EMOTION

POSSIBLE MECHANISM OF DEATH FROM FRIGHT

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and
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The expression "frightened to death" or "scared to death" has been handed down generation after generation. It is still in common use today and is, indeed, quite descriptive of the emotions produced by unusual or extraordinary fright. A particularly harrowing experience is vividly described when one says, "It scared the life out of me."

Have people actually been "scared to death?" It is common knowledge that fright may have varied effects on a person, e. g., tachycardia, palpitation, increased sweating, weakness, tremor of hands or voice, and syncope. Certainly patients with heart disease, such as coronary artery disease, have suddenly died after some fright or other similar emotional upset. The usual mode of death is attributed to ventricular fibrillation.

We have observed patients with underlying heart disease in whom emotional excitement precipitated ventricular tachycardia. One of these was a man with coronary artery disease and an old myocardial infarct. He had had numerous attacks of proved ventricular tachycardia. A common "trigger" mechanism for such an arrhythmia was a heated argument with his son or wife. Another patient with congenital heart disease (Eisenmenger's complex) was fond of watching midget auto races. Ventricular tachycardia occasionally occurred coincident with the excitement produced when cars skidded around the curves.

The sequel of ventricular fibrillation and death following ventricular tachycardia is documented, clinically and experimentally.

Escamilla [1] described a patient whose electrocardiograms clearly illustrated the transition from ventricular extrasystoles to ventricular tachycardia, which in turn was followed by ventricular fibrillation. Ventricular arrhythmias such as extrasystoles, tachycardia and fibrillation have been produced by injections of epinephrine in normal animals.[2] The development of these disturbances in rhythm is further enhanced when the animal is anesthetized, particularly with chloroform and cyclopropane.[3]

Normal persons may exhibit various cardiac abnormalities due to emotional stimuli. Extrasystoles, usually ventricular, are common. Sinus tachycardia, paroxysmal auricular tachycardia, paroxysmal auricular fibrillation, and conduction disturbances are known to occur. Extrasystoles are commonly associated with even minor emotional strain. One of us observed frequent premature contractions prior to presenting a paper at a medical meeting. The rhythm became regular coincident with the beginning of the talk.

There is physiological and pathological evidence of importance. The work of Brow, Long, and Beattie [4] showed in experimental animals that there is a nervous pathway from the hypothalamus to the heart that could bring forth various types of ventricular irregularities, such as extrasystoles, tachycardia, and ventricular fibrillation, and death. Inasmuch as the hypothalamus is regarded as the seat of emotions, this work forms a reasonable background for the hypothesis of production of ventricular arrhythmias as the direct result of emotional upsets. It is conceivable that in a normal person a highly emotional situation such as severe fright could produce more serious arrhythmias, such as runs of ventricular tachycardia, even terminating in ventricular fibrillation and death. Such a chain of events could tie in with the sudden release of epinephrine with the resultant myocardial actions as shown experimentally in animals. This would lend support to the truth of the expression "frightened to death." We believe such a mechanism, admittedly rare, is possible, as illustrated by the following case.

REPORT OF A CASE

P. S., a 29-year-old unmarried woman, was admitted to the Peter Bent Brigham Hospital with a two-year history of "attacks" characterized by difficulty in getting her breath, "smothering sensation," palpitation, nervous tension, weakness, and a feeling that her "circulation had gone dead." These episodes sometimes lasted two hours, were unrelated to food, and were unassociated with syncope. The attacks increased with such frequency that she had to stop her work as a draftswoman and seek medical help. Family history was important only in that her father died at the age of 50 after a cerebral vascular accident. Her past history revealed no specific cardiovascular abnormality. There was no history of rheumatic fever and no known heart disease, murmurs or hypertension. Results of physical examination were likewise unremarkable. The blood pressure was 110/60. She was tall, thin, well developed, and in no distress. Her face was flushed and the skin soft and moist. The thyroid was normal, and the lungs were clear. The heart was not enlarged. Rhythm was regular, and sounds were of good quality. P_2 was slightly greater than A_2. No murmurs were heard except for an insignificant grade 2 pulmonic systolic murmur. The remainder of the physical examination was noncontributory. All laboratory data were normal including results of roentgenographic and fluoroscopic examination of the heart, electrocardiograms, intravenous glucose tolerance test, and postural and carotid sinus tests. Hyperventilation did not produce

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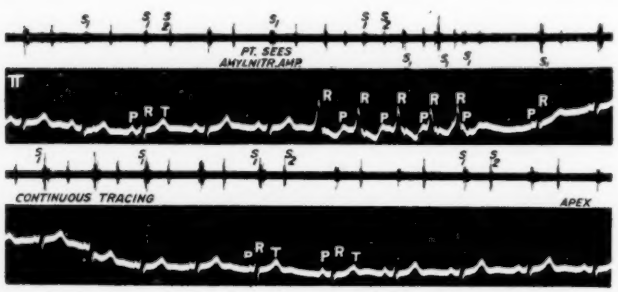
one of her episodes. An epinephrine tolerance test for pheochromocytoma elicited negative results. No electrocardiograms were made during the test, but, after the subcutaneous injection of 0.5 cc. of epinephrine, the patient's pulse rate rose from 110 to 162 and her blood pressure from 120/70 to 140/70. She complained of palpitation and profuse sweating of the hands, followed by numbness and coldness of the hands and feet. She felt "trembly."

No organic disease could be found to account for her complaints. She was therefore referred to the psychiatrist for evaluation. It was felt that she had an anxiety conversion hysteria somatic reaction and needed supportive psychotherapeutic interviews to give her some educational insight into her current emotional problems. She was described as being a "bright, articulate, but strikingly immature person." "At the present time she is panicky, tense, and troubled." Intensive psychoanalysis was thought to be necessary to really dissolve her multiple conflicts, and arrangements for psychiatric treatment were made.

The patient's hospital stay coincided with studies of the effect of amyl nitrite on normal heart sounds. She, along with about 12 other patients, volunteered for the test. She was the last patient, and, when it was her turn, it was noted that she was extremely apprehensive. The procedure was therefore explained in detail to reassure her that no pain or harmful effects would occur. (Continuous phonocardiographic tracings were recorded before, during, and after inhalation of amyl nitrite.) She had heard the "pop" sound coincident with breaking of the amyl nitrite pearl



This tracing shows a brief paroxysm of ventricular tachycardia (five consecutive premature ventricular beats) that occurred as soon as the patient saw the amyl nitrate ampule. (From Harvey, W. P., and Levine, S. A.: Clinical Auscultation of the Heart, Philadelphia, W. B. Saunders Company, 1949.)

when the preceding patients on the ward were tested, and she was likewise reassured as to the benignity of the procedure.

She stated that she understood, but her apprehension obviously remained. She carefully watched each step. A preliminary examination of her heart revealed no abnormality. A complete set of electrocardiograms was taken, which showed normal curves. Finally, the phonocardiograph was connected and a continuous strip on lead 2 was started. While the tracing was running, the small tin box containing the pearls of amyl nitrite was brought out. Her eyes were focused on the box, and the instant she saw the pearl a short burst of rapid beats was heard, followed by a return to the original rhythm. The pearl was not broken. As shown on the phonocardiogram in the accompanying figure, a short paroxysm of ventricular tachycardia had taken place. The patient sensed the change in rhythm and said it was similar to the type of palpitation she had noted in the past. From her history it was inferred that she may have experienced episodes of extrasystoles and tachycardia.

COMMENT

The interesting feature of this case is the development of paroxysmal ventricular tachycardia on an emotional basis. It is conceivable that in this type of patient a stronger emotional stimulus, such as severe fright, could be followed by more prolonged ventricular tachycardia and, in turn, ventricular fibrillation and death.

An interesting correlation to this discussion is the so-called voodoo death. Here, the problem is similar, in that emotional stress (fear or terror) may be the cause of a chain of events leading to death. The analogy differs in that "voodoo" death may be a gradual process (involving perhaps days) rather than a sudden occurrence.

"Voodoo" death, according to Cannon,[5] has been reported by competent observers. Such a mode of death induced by fright or fear follows the "hexing" of the subject by the "medicine man" or by "black magic." It has been reported among the native tribes of South America, Africa, Australia, New Zealand, and the Pacific islands. A common example of "voodoo" death in the ignorant, superstitious native is quoted from Cannon's interesting article.

> A young negro on a journey lodged in a friend's house for the night. The friend had prepared for their breakfast a wild hen, a food strictly banned by a rule which must be inviolably observed by the immature. The young fellow demanded whether it was indeed a wild hen, and when the host answered "No," he ate of it heartily and proceeded on his way. A few years later, when the two met again, the old friend asked the younger man if he would eat a wild hen. He answered that he had been solemnly charged by a wizard not to eat that food. Thereupon the host began to laugh and asked him why he refused it now after having eaten it at his table before. On hearing this news the negro immediately began to tremble, so greatly was he possessed by fear, and in less than twenty-four hours was dead.

Cannon offers a physiological explanation of such experiences.

SUMMARY

A case is described in which an emotional upset immediately precipitated a short paroxysm of ventricular tachycardia. This was confirmed by continuous electrocardiographic tracing before, during, and after the episode. The patient had no evidence of organic disease but had complained of a good deal of palpitation for the previous two years. Inasmuch as this type of arrhythmia may be a prelude to ventricular fibrillation and death, it throws light on a possible mechanism of "death from fright."

5. Cannon, W. B.: "Voodoo" Death, Am. Arthropologist 44: 169-181, 1942.

The Amateur in Radiation Therapy.—In radiation therapy the doses are now larger than ever but this increase is deliberate and, paradoxically, the patient is safer now than he used to be and less apt than formerly to suffer unfavorable side effects. This has resulted largely through the abolishment of the concept of the "air dose" and the substitution of the concept of the "tissue dose." A skillful and experienced team of physicians and physicists equipped with modern radiologic tools can with safety deliver large and precisely measured doses of radiation to sharply localized blocks of neoplastic tissue and yet spare neighboring structures that are thought to be normal or are known to be essential to the patient's survival. This development is of immeasureable importance to cancer patients but it has wiped out any place there may ever have been for the amateur worker in radiation therapy. I wonder sometimes whether a tacit recognition of this fact may account for the unfortunate increase in the employment of radiation for the treatment of bursitis, arthritis and other nonmalignant diseases. It is true that some qualified therapists do advocate such treatment but I suspect that many of its advocates are physicians who, having invested in therapy equipment, now recognize their inability to deal with neoplasms but hope that the old air dose techniques are still sufficiently good for the treatment of nonmalignant conditions. —P. C. Hodges, M.D., The Cumulative Effects of X-Ray Exposures, *Postgraduate Medicine*, August, 1952.

SPECIAL ARTICLE

This is the second of a series of articles prepared from the viewpoint of the general practitioner, at the request of the Advisory Council on Professional Education of the Commission on Chronic Illness. Statements and conclusions by the author do not necessarily represent the opinion or policy of the Commission.

CHRONIC ILLNESS AND SENESCENCE

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Modern techniques applied in both preventive and curative therapy against the acute exogenous and largely infective diseases of infancy, childhood, and youth have immensely reduced mortality in the early years of life. In the United States in the year 1900 the average life expectancy at birth was 47 years; in 1951 boy babies had an average life expectancy of more than 67 years and girl babies an expectancy of over 71 years. This increment in longevity of over 20 years in half a century, dramatic as it is, is not an unmixed blessing. The toll of prolonged disability of varying degree consequent to chronic illness is so immense as to be truly immeasurable. The burdens of chronic disease, both individually and collectively, are the source of greater tragedy than death from acute illness.

The problems of chronic illness and those engendered by the increasing number of the aging and aged in our population are not identical, but the two areas overlap extensively. Aging per se does not necessarily imply chronic illness, but most of the disablement, misery, and uselessness of those past the so-called prime of life are consequent to chronic progressive disease and not to age alone. Chronic illness is, of course, not limited to those in the senescent period of life. Nevertheless, both the incidence of chronic illness and the degree of disability therefrom are markedly increased after age 40. At age 30 approximately 6 persons per thousand are chronically invalided; at age 40 10 per thousand; at age 50 15 per thousand; at age 60 28 per thousand; and at age 70 about 50 per thousand.[1] According to the Metropolitan Life Insurance Company's studies,[2] in the year 1901 approximately 53.5% of all deaths were due to chronic disease, whereas in 1945 the chances of ultimately dying from chronic disease (instead of from acute disease, external violence, and all other causes) had increased to 82%.

Impressive as these figures are, they still fail to reveal the full present and impending significance of long-term illness in the health problems of today. Mortality data, viewed alone, can be most misleading. Morbidity, degree of disability, and duration of chronic invalidism are equally important criteria.[3] Data regarding the incidence of the various long-term disorders are few and, for the most part, unsatisfactory. Much information is now being accumulated. All previous estimates of the prevalence of such conditions as vascular disease, diabetes, and arthritis are grossly misleading in that they revealed, at most, only the known, discovered, diagnosed cases in which symptoms of sufficient intensity to demand clinical attention were already manifest. Certain recent studies indicate that there may be as many as 2 million diabetics in the United States, about half of whom are unaware of their illness. The number of impending, potential, or borderline cases is probably even larger. In many respects, the undiscovered cases represent the greater challenge to the medical profession, for the earlier in the course of the chronic progressive disorders therapy is instituted, the better the chances of significant accomplishment. This is obviously true of malignant neoplasms; it is equally applicable to arteriosclerosis, hypertensive disease, aplastic anemia, and the arthritides.

Total invalidism involving bed or institutional care represents but a small fraction of the total load of disablement, suffering, lost productivity, and economic loss engendered by long-term illness. The loss from partial impairment is incalculable.[4] The losses due to impairment of efficiency of personnel not sick enough to be absent but who accomplish but a fraction of the work they are potentially capable of because of chronic impairment of health by such conditions as anemia, hypertension, and neglected cholecystitis are probably many times more than those attributable to actual time lost.[5] As yet, it has been impossible to measure such waste in human productivity with any degree of accuracy.

The whole pattern of disease in relation to morbidity, mortality, and the duration and severity of disability has changed markedly in the last 50 years. These changes are continuing. They affect profoundly the future practice of medicine.[6] One aspect of the shift in the character of disease is revealed by a comparison of the six leading causes of death in 1900 and in 1951 (table 1).[7]

Particularly notable is the fact that in 1900 the three most important causes of death were diseases of infectious origin, but in 1951 the three major sources of death were noninfective, so-called degenerative disorders. If cerebral vascular accidents are included with diseases of the heart, as they should be, because they are both due to vascular disease, in 1951 cardiovascular disorders accounted for more than 300 deaths per year per 100,000 of the population.

The National Heart Institute [8] reports that in 1951 cardiovascular diseases accounted for 51.8% of deaths from all causes, and that arteriosclerosis and hypertensive arterial disease caused over 90% of deaths due to cardiovascular disorders. It is notable that in 1951 only 3% of deaths resulted from rheumatic fever and chronic rheumatic heart disease.

However, evaluation of the significance of various disease groups, on the basis of mortality data alone, are mis-

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Chairman, Advisory Council on Professional Education, Commission on Chronic Illness.

1. The National Health Survey, 1935-36: The Magnitude of the Chronic Disease Problem in the United States, Sickness and Medical Care Series, Bulletin No. 6 (revised), Division of Public Health Methods, National Institute of Health, U. S. Public Health Service, 1939.
2. Dublin, L. I.: Statistical Bulletin No. 29, New York, Metropolitan Life Insurance Co., July, 1948, p. 9.
3. Geriatric Medicine: The Care of the Aging and the Aged, edited by E. J. Stieglitz, ed. 2, Philadelphia, W. B. Saunders Company, 1949, chap. 1.
4. Frank, L. K.: Human Conservation: Story of Our Wasted Resources, National Resources Planning Board, March, 1943.
5. Stieglitz, E. J.: Senescence and Industrial Efficiency, Indust. Hyg. Found. of America, Proc. 8: 57, 1943.
6. Stieglitz, E. J.: A Future for Preventive Medicine, New York, Commonwealth Fund, Division of Publications, 1945.
7. Excellent Health Record in 1951, Statistical Bulletin, Vol. 33, No. 1, New York, Metropolitan Life Insurance Co., Jan., 1952, p. 1.
8. National Heart Institute Circular No. 7, National Institutes of Health, U. S. Public Health Service, Oct., 1951.

leading. Of equal, if not greater moment, are the elements of severity and duration of disability. For example, chronic hypertrophic arthritis, asthma, psychoneurosis, and schizophrenia disable many thousands of persons, but are rarely fatal. Though arteriosclerotic dementia is often associated with fatal cardiovascular accidents (cerebral or coronary) many years of institutional care may be necessary because of psychiatric invalidism before the fatal termination. At present one estimate [9] states that for about 40% of persons admitted to mental hospitals the diagnosis is arteriosclerotic and/or senile psychosis. According to the National Institute of Mental Health [10] 32% of all persons admitted for the first time to state mental hospitals in 1949 were aged 60 or over.

Chronic illness may arise at any age and persist for many years, through maturity and senescence into senility. Furthermore, partially disabling sequelae of acute diseases in youth may last for many years. The crippling handicaps left as sequelae of early acute illness are usually fixed and nonprogressive. For example, the mechanical handicaps consequent to poliomyelitis are not progressive and thus permit development of compensatory capacities that diminish the actual disability. Rheumatic heart disease is a significant exception, however, to the general rule. On the other hand, the disorders that commonly are manifested in later maturity (after 40), the so-called "degenerative diseases," are characteristically progressive, leading slowly to functional depreciation. It is with these disorders that I am particularly concerned in the present discussion.

TABLE 1.—*Comparison of the Six Leading Causes of Death in 1900 and 1951*

1900			1951		
Rank	Cause	Rate per 100,000	Rank	Cause	Rate per 100,000
1.	Tuberculosis	195	1.	Heart disease	240.7
2.	Pneumonia	176	2.	Malignant neoplasms	120.8
3.	Diarrhea and enteritis	140	3.	Vascular lesions of the central nervous system	64.5
4.	Heart disease	137	4.	Accidents	38.4
5.	Nephritis	89	5.	Pneumonia and influenza	18.2
6.	Accidents and violence	88	6.	Tuberculosis	17.6

DEFINITION OF CHRONIC ILLNESS

Chronic illness by definition means impairment of health over a protracted period of time. It does not necessarily imply a specific disease entity. Nor does the term require that the illness be associated with gross or detectable disability or even awareness of the existence of a disorder. The Section on Chronic Diseases and the Aging Process of the National Health Assembly in 1948 [11] formulated the following working definition for the term chronic illness: "Any impairment in health which persists, regardless of whether or not the patient is aware of its existence and irrespective of the degree of disability it induces, its tendency to progress or its rate of progression." Implicit, however, in this definition are the characteristics of variable onset, varying from obvious to so highly insidious that the onset can not be dated, progressiveness, and variable disability. The actual onset of the disorder may precede awareness by many years. This is typically illustrated by diabetes mellitus and/or arteriosclerosis.

Health, like age, is relative. There are degrees of health just as there are degrees of illness, or intelligence, or equanimity, or beauty. Health is an abstraction or ideal. Perfect health is probably unattainable, though it may be approached. Unfortunately, the antiquated, negativistic definition of health as "that state of existing in the absence of disease" is still to be found in some medical dictionaries. Let us redefine health as having quantitative attributes and perfect health as that state of being in which all the functional capacities of the organism have maximum reserves. Optimum health is affected by age. The adolescent or young adult may have maximum cardiac and muscular vigor, but the intellect has not as yet developed to its peak. By the time intelligence and emotional homeostasis are fully developed, somatic depreciations will have reduced other functional capacities to below optimum levels.

The relativity of health is particularly significant in dealing with mature persons. Normal is a vague and misleading term. The commonest connotation is that "normal" is nearly synonymous with "average." Average certainly does not imply optimum. Thus, normal health and optimum health are frequently widely divergent.

Modern medical education has been concerned chiefly with teaching physicians to identify and treat disease entities. It is only recently that attention has been focused on the individual, who may or may not be suffering from an identifiable disease. Pediatrics and psychiatry are the two fields of medical practice in which concern with the patient rather than with his disease has met with the least resistance and inertia.[12]

NATURE OF CHRONIC DISORDERS IN SENESCENCE

The major chronic disorders associated with senescence, both in incidence and in pathogenesis, are the so-called "degenerative diseases." Obviously, these are not the only chronic diseases met with in persons past the meridian of life, for chronic infections such as tuberculosis and syphilis are not uncommon. Nevertheless, the following chronic progressive disorders constitute the primary problem in connection with chronic illness and senescence:

A. Circulatory disorders
   1. Chronic infective myocardial disease, both rheumatic and luetic
   2. Hypertensive arterial disease
   3. Arteriosclerosis,
      (a) Cerebral, with associated apoplexy, dementia, or encephalopathy
      (b) Coronary, with associated cardiac disease
      (c) Renal, with associated chronic nephritis
      (d) Pancreatic, with associated diabetes mellitus
      (e) Of the extremities, with associated gangrene or Buerger's disease
   4. Combination forms

9. The Problems of the Aged Patient in the Public Psychiatric Hospital, Report No. 14, Topeka, Kan., Committee on Hospitals, Group for the Advancement of Psychiatry, Aug., 1950.

10. Mental Health Statistics, Current Reports, National Institute of Mental Health, U. S. Public Health Service, Series IMH, B52, No. 1, Dec., 1951.

11. America's Health, The National Health Assembly, 1948, New York, Harper & Brothers, chap. 4, p. 91.

12. Geriatric Medicine: The Care of the Aging and the Aged, edited by E. J. Stieglitz, ed. 2, Philadelphia, W. B. Saunders Company, 1948, chap. 6.

B. Metabolic disorders, including diabetes mellitus, anemia, the climacteric (both female and male), and gout

C. Malignant tumors, all forms

D. Arthritides

Of these, the first two groups, the circulatory and metabolic disorders, are preeminently important. They are so intimately related that attempts to separate the consequences into distinct and isolated disease entities are futile.[13] It may be worth while to briefly consider some of their generic characteristics, for these affect practice significantly.

The essential differences between the disorders common to youth and those typical of later life are perhaps best contrasted in tabular form (table 2).[14] The most important of these generic characteristics from the point of view of the practicing physician are (1) the silence and insidiousness of onset, (2) the multiplicity and variability of etiological factors involved, (3) the tendency to persistent progression, and (4) the common superimposition of several disorders in the same person.

As these disorders begin asymptomatically and may be well advanced before symptoms are sufficiently unpleasant to cause the patient to seek relief, they must be searched for in apparently well people to be discovered early enough to be amenable to therapy. The clinical picture, when symptoms do develop, is confused by the fact that almost invariably the symptoms are not directly referrable to the basic lesions of the disease. For example, there is no kinesthetic sense that informs the patient of hypertension. Symptoms are consequent to impairment of circulation, and therefore of the nutrition, of one or more parenchymatous structures. Functional depreciation is most insidious and evidences of functional failure producing symptoms do not occur until the functional capacity falls below the minimum requirements for the maintenance of homeostasis. Thus early detection, which is essential for early and effective therapy, involves evaluation of functional reserve capacities. Depreciations in reserve capacity (cardiac, renal, and metabolic) can be detected only by stress tests, unless the depreciation is so great that it is usually irreparable and irrevocable. The lesson to be remembered is that we must search for these silent, insidious, fifth column disorders in apparently well people and not wait until they become obvious by overt lesions.[15] Health is always relative, and the borderline between health and disease vague and indefinite.[16]

The multiple and variable etiology of these disorders is of the utmost significance to the clinician. None of these disorders arises from a single cause. In sharp contrast to the exogenous and usually infective disorders of youth, these diseases are endogenous and result from the accumulative effects of several superimposed and protracted sources of injury. In no two instances of any one of these disorders is the etiology necessarily identical. No one will ever discover "the cause of" hypertensive disease, arteriosclerosis, or cancer. Hypertension may be due to chemical intoxication due to renal failure, arsenic, or endocrine imbalance, due to lesions of the central nervous system, or secondary to prolonged emotional tension from repressed and distorted resentments.[17] Likewise, each neoplasm is a different disease: the etiology of cancer of the skin, cervix, breast, rectum, or stomach is not the same, though there may be certain factors common to all instances. It is significant that several known factors may contribute to the causation of several of the degenerative processes. For example, obesity is a factor in the genesis and adverse prognosis in such diseases as diabetes mellitus, cancer, hypertensive disease, and cholecystitis.[18]

Causation always involves three groups of factors: predisposing, provoking, and perpetuating influences. The relative weight of these factors varies in different diseases and in different instances of the same disease. For example, perpetuating forces are immeasurably significant in the complex riddle of cancer, for the greatest obstacle to curative therapy is the diabolically persistent continuation of growth and metastasis.[16b] Similarly, in hypertensive disease the perpetuating influence of medial hypertrophy is a potent antagonist to effective therapy.[19] Both diagnosis and therapy are severely handicapped by the multiplicity and variability of etiological factors and by our ignorance of factors as yet undiscovered. Each instance of degenerative disease constitutes a complex research problem requiring the most thorough search into history and genetic background, mode of life, and metabolic dyscrasias in order to suggest causation. Effective therapy, whether preventive, curative, or for the purpose of control and retardation of a progressive disorder, is predicated on an understanding of etiology.[20] At best our conclusions as to causation are tentative and incomplete. Nevertheless, continued search for contributing fac-

TABLE 2.—*Comparison of Characteristic Disorders in Youth and Senescence*

Youth	Senescence
Etiology	
Exogenous	Endogenous
Obvious	Occult
Specific (single)	Cumulative
Recent	Distant in time
	Multiple (superimposed)
Onset	
Florid	Insidious; asymptomatic
Course	
Acute	Chronic
Self-limited	Progressive (long disability prior to death)
Immunizing	Not protective (increased vulnerability to other diseases)
Little individual variation	Great individual variation
Usually a single disease	Typically overlapping of several disorders

13. Stieglitz, E. J.: Difficulties in the Clinical Recognition of Degenerative Diseases, in Biological Symposia XI: Aging and Degenerative Diseases, edited by R. A. Moore, Lancaster, Pa., Jaques Cattell Press, 1945.

14. Stieglitz, E. J.: Symposium on Treatment of Long-Term Illness: Medicine in an Aging Population, M. Clin. North America **33**: 295 (March) 1949; The Rationale of Geriatric Medicine, Ann. Int. Med. **35**: 848 (Oct.) 1951.

15. Footnote 12. Stieglitz, E. J.: Problems in Geriatric Medicine: The Periodic Health Inventory, Clinics **4**: 1322 (Feb.) 1946.

16. (*a*) Stieglitz.[6] (*b*) Stieglitz, E. J.: The Second Forty Years, Philadelphia, J. B. Lippincott Company, 1946.

17. Weiss, E.: Emotional Factors in Cardiovascular Disease, Springfield, Ill., Charles C Thomas, Publisher, 1951. Weiss, E., and English, O. S.: Psychosomatic Medicine: The Clinical Application of Psychopathology to General Medical Problems, ed. 2, Philadelphia, W. B. Saunders Company, 1949.

18. The Influence of Overweight on Health and Disease, New York, Metropolitan Life Insurance Co., 1951.

19. Stieglitz, E. J.: Arterial Hypertension, New York, Paul B. Hoeber, Inc., 1930.

20. Stieglitz.[6] Footnote 12.

tors is vitally significant and can mean the difference between therapeutic failure and success.

Progression, a most significant generic characteristic of all these disorders, is frequently slow but typically persistent. None of these disorders shows a significant tendency to be self-limited; neglect accelerates progression. Thus early detection and prompt institution of a therapeutic regimen are essential for therapeutic effectiveness. The slowness of progression (particularly with cardiovascular disease, the metabolic disorders, and the arthritides) gives the physician ample opportunity for complete and thorough diagnostic study and application of therapeutic measures to control the disorder with the hope of arresting the progression. Early in hypertensive disease, for example, there is no immediate jeopardy. However, because of the asymptomatic early course of these disorders, they are too rarely identified early enough. Late, when symptoms and signs are obvious and the patient is already partially disabled, the effectiveness of treatment is greatly reduced.

The objectives of therapy are modified by the character of these disorders. Cure, in the absolute sense, is usually impossible, for irreversible changes have occurred during the long, silent early phases. Control, as illustrated by therapy in diabetes mellitus, hypothyroidism,[21] the climacteric, and hypertensive disease,[22] is more frequently the objective. Often the maintenance of a status quo is a significant therapeutic accomplishment. The patient should be instructed concerning the progressive nature of these disorders and thus made aware that arrest of progression is important. Frank honesty as to the limitations of therapy can prevent much of the pathetic "shopping around," anxiety, and discontent so frequently observed in senescent persons with chronic illness. It is most unwise, as well as intellectually dishonest, to promise more than there is good reason to believe can be accomplished.[23] On the other hand, it is never justifiable to pass off a complaint as being an inevitable consequence of age, to say "Well, what else can you expect at your age?" Partial rehabilitation and improvement are always possible and frequently dramatic.[24]

Motivation for the efforts requisite for improvement is of primary importance. Without the will to improve health, little can be accomplished. The will merely to survive does not suffice: this may only perpetuate chronic disablement. The person with long-term illness will make strenuous effort to improve his health only if there is adequate motivation for so doing. Humans will not make an effort to jump out of an uncomfortable situation until they can see a place to land which seems to be more comfortable and happier than where they are. The hazard that martyrdom may be a source of pleasure must always be kept in mind. Martyrs are martyrs largely by unconscious choice. The handicapped person will not exert himself toward rehabilitation if there is no place in society where he may find the satisfaction of usefulness. Rehabilitation is impossible without effort on the part of the patient; effort will not be expended without adequate motivation supplied by the promise of greater happiness. The management of long-term illness involves psychological, sociological, and economic questions as well as purely clinical therapeutics. There is serious hazard in making the facilities or institutions devoted to the care and improvement of long-term sickness too desirable or too comfortable. Disability in any form must not be a source of profit or satisfaction.[25]

Motivation is of particular significance with the preventive aspects of chronic illness. Largely because of the endogenous character of the etiology, wholesale or public health methods are not applicable to the prevention of the chronic progressive disorders of later maturity.[6] No amount of sanitary control of water and food supplies can reduce the incidence of diabetes mellitus; the control of obesity is chiefly a matter of individual self-control. Education must play an increasingly major role in both prevention and control of these progressive chronic disorders. There can be no disagreement with the statement that the most important elements in the successful management of diabetes mellitus, tuberculosis, and heart disease are the understanding of the nature of the disorder by the patient and the conscientiousness of his cooperation. More and more the physician-patient relationship must become a teacher-student relationship.[26]

Superimposition of several chronic, so-called degenerative disorders in the same patient is the rule rather than the exception. These disorders do not confer immunity but increase the vulnerability of the patient to related diseases. The primary changes in the circulatory disorders arise in the matrix or supporting structures, though the critical injury is to various parenchymal cells.[27] Several of the endocrine and metabolic difficiencies arising late in life (late diabetes mellitus and hypothyroidism) are probably secondary to vascular impairment of the glandular structures. Thus arteriosclerosis contributes to the genesis of diabetes, whereas the metabolic impairment of the latter aggravates the vascular change.

The damage done to parenchymal cells is essentially an interference with cellular nutrition. A broad concept of nutrition must include not merely the ingestion of nutriments, but their effective absorption and transportation. Furthermore, oxygen is just as much a nutriment as glucose and equally necessary; water is as vital as any vitamin. The vascular system is concerned with food transport and the removal of metabolic debris. These disorders impair parenchymal nutrition by any one or more of the following mechanisms[13]: (1) inadequate supply, (2) ineffective transport, (3) inefficient utilization, or (4) insufficient removal of metabolic debris. These factors are intimately interrelated and frequently overlap. For example, histanoxia, or cellular oxygen want, may be induced by a combination of lowered oxygen-carrying capacity (anemia, perhaps of nutritional

21. Kimble, S. T., and Stieglitz, E. J.: Hypothyroidism: A Geriatric Problem, Geriatrics **7**: 20 (Jan.-Feb.) 1952.

22. Stieglitz, E. J., in The Diagnosis and Treatment of Cardiovascular Disease, edited by W. D. Stroud, ed. 4, Philadelphia, F. A. Davis Company, 1950, chap. 34.

23. Stieglitz.[16] Footnote 12.

24. Warren, M. W.; Kountz, W. B.; Pratt, L. A., and Stieglitz, E. J.: Geriatric Medicine: Therapeutic Aspects: A Panel Discussion, J. Gerontol. **7**: 100 (Jan.) 1952.

25. Stieglitz, E. J.: The Integration of Clinical and Social Medicine, in Social Medicine: Its Derivations and Objectives, edited by I. Galdston, Proceedings, Institute on Social Medicine, New York Academy of Medicine, 1947, New York, Commonwealth Fund, Division of Publications, 1949.

26. Proceedings of Conference on Chronic Illness: Preventive Aspects, Chicago, March 11 to 14, 1951, Commission on Chronic Illness, to be published.

27. Cowdry's Problems of Aging: Biological and Medical Aspects, edited by A. I. Lansing, ed. 3, Baltimore, the Williams & Wilkins Company, 1952.

deficiency origin), arteriolar constriction and capillary stasis as in hypertension, and partial cardiac incompetence. The net result is asphyxia of parenchymal elements. Perhaps, because of hypoinsulinism, glucose combustion is further impaired. Primary malnutrition, including both deficiencies and excesses in the habitual dietary, is very common in later years and a most significant element in depreciation of health.[28] The commonest deficiencies are related to protein, calcium, iron, and water intake. Impaired absorption, fixed dietary habits, mechanical difficulties with mastication, and many other factors contribute to the complexity of the therapeutic problems.

As consequences of these generic characteristics clear-cut, clearly defined, and single clinical entities are rarely observed in aging and/or aged patients and great variability in both manifestations and course is to be expected. Rates of progression vary widely. It is still not known why arteriosclerosis in one person affects the coronary vessels more than other arteries or why in another the cerebral vessels appear to be most involved. Whether the difference lies in the disorder or in selective vulnerability of the individual is an open question. The great variations in distribution and intensity of the lesions of arteriosclerosis accentuate the importance of individualization in diagnostic study and therapy of senescent persons. Variability undoubtedly depends in some way on the fact that each person has been subject to a different series of insults and injuries in different sequence. The cumulative effects of the innumerable intoxications and vicissitudes of our existence probably play a major role in determining the vulnerability of this or that structure.

Chronic illness in later maturity is greatly affected by prior injuries. Every toxic, psychic, or traumatic experience leaves some residue of scarring behind. The detriment may or may not be apparent or even detectable. Revelation of the consequences may be long delayed. For example, we do not actually see the cloudy swelling of parenchymatous tissues associated with fever, though we know it occurs and that subsidence of the acute febrile intoxication does not imply immediate or perfect repair of this damage. Every such injury leaves some minor residue. Individually they may appear to be negligible, but their accumulative significance is considerable.

These various characteristics of the common chronic progressive disorders seen in senescent persons emphasize the following basic principles: 1. Health is always relative. This is particularly conspicuous in later maturity. 2. Impairment in health in later years results from the accumulated injuries of previous detrimental experiences as well as from more specifically delineated disease entities. 3. The degenerative diseases are characterized by: (*a*) silent, insidious onsets, (*b*) multiple and variable etiology, (*c*) persistent progression that may vary widely in rate, (*d*) a pathogenesis involving impairment of parenchymal cellular nutrition and metabolism though the primary lesions are in the matrix tissues, and (*e*) great individual variation in manifestations and course. 4. Superimposition of several progressive disorders in later maturity is the rule rather than the exception. 5. Individualization in diagnosis (particularly as diagnosis pertains to etiology) and especially in therapy is essential. The patient must be treated as an individual in impaired health. To focus therapy on the disease or diseases is insufficiently comprehensive and invites therapeutic failure. The individual is indivisible.

ATTACKING THE PROBLEM

Obviously the problems of chronic progressive disease in senescence are so immense and complex, involving the application of many disciplines, that it is difficult to know just where and how to attack the situation. Perhaps the confusing situation may be somewhat clarified by asking, and attempting to answer, two questions: First, what are the objectives, and, second, who is responsible for what?

The objectives may be tentatively enumerated in the order of their probable importance as follows:

(1) prevention; (2) control and retardation of progression; (3) rehabilitation, including the somatic, psychological, and socioeconomic facets of disability (this is less than cure but much more than palliation); and (4) care of nonremedial disabled persons, including the somatically disabled and the psychiatrically disabled.

The responsibility for attaining these objectives may be logically subdivided among society, maturing and senescent persons, the real or potential victims of progressive chronic illness, and medical science and practice.[6] It is with the last of these that I am primarily concerned at the moment, but the other areas of responsibility must not be ignored.

By the responsibilities of society I mean those obligations that properly rest on the population as an aggregate group. This includes all official governmental (federal and local) agencies properly involved in health, voluntary organizations concerned with health and the care of the sick, private national and local professional associations, schools, colleges, universities and medical schools, philanthropic foundations, including hospitals and clinics, and industry. Of the latter the insurance business, industrial health organizations, labor unions, and the food and pharmaceutical industries are most particularly involved.[6] Their major tasks are to foster and support (1) research; (2) education, both lay and professional[26]; (3) facilities (laboratories, clinics, and hospitals) for the better application of existing medical knowledge; and (4) sanitary control of food, water, and quarantine (public health service).

The control, prevention, and retardation of the common and increasingly significant degenerative diseases can be accomplished only by individual attention and guidance. Wholesale measures can not suffice. Health in later years can neither be given nor bought. It must be earned. Health is not an inherent right, but a privilege, and, as a privilege, is inseparable from responsibility. The individual can not escape responsibility for his own health in later maturity no matter how much pampering paternalism may encourage him to avoid acceptance of personal responsibility. We are all sadly aware of how feeble is the sense of personal responsibility in many. The last 20 years have done much to destroy this sense and the feeling of pride involved in the acceptance of responsibility. Nature does not condone nor forgive violation of her laws of wise living, even if the violations be due to

28. Stieglitz, E. J.: Nutrition Problems of Geriatric Medicine: Council on Foods and Nutrition. J. A. M. A. **142**: 1070 (April 8) 1950.

ignorance. Unquestionably, recurrent abuse of the biological organism in many different ways plays a significant role in the genesis of many of the progressive chronic disorders so characteristic of later maturity.

The inescapable responsibilities of the mature person in regard to his health include the following points as a minimum list: (1) effort to learn how to use rather than abuse his inherited endowment of a fairly healthy body and mind; (2) effort to seek periodic inventory of his health status, with the motive of constructing greater health, detecting asymptomatic disease in its incipiency, and correction of defects and unwise habits [17]; and (3) conscientious effort to meticulously follow the advice of his physician, often involving application of considerable and uncomfortable self-discipline (as in weight reduction in obesity). Without these individual efforts the science and practice of medicine can do little to alleviate the growing toll of prematurely disabled senescent persons.

The responsibilities of medical science and practice can be divided into three major categories: (1) research; (2) education; and (3) practice. Here is not the place to elaborate on the urgent needs for research into the fundamental biological processes of aging as they affect both the soma [28] and the psyche [29] of man.

Responsibility for education, however, should be the immediate concern of every physician and not only of those making teaching their primary activity. New knowledge is of little value unless it be disseminated to those who make it pragmatic by application. Education, in relation to the problems of chronic illness in senescence, involves three major areas [26]:

(1) education of physicians and dentists at all levels, including undergraduate, graduate (interns and residents), and postgraduate study; (2) education of ancillary professional personnel such as nurses, physical therapists, social workers, clinical psychologists, and hospital administrators; and (3) education of the lay public at all ages.

The practicing physician oftener than not is only indirectly involved in the first two of these categories. His daily and continuous contact with the lay public (his patients), however, places him in a most significantly advantageous position to teach. The medical profession as a whole has been most remiss in accepting its responsibility for informing the public in matters of health. All too often this is left to lay writers who, without adequate knowledge of their subjects, sin greatly by omission as well as commission in trying to make the material acceptable. Physicians have avoided both direct individual and indirect teaching of their patients and the public at large for several reasons. In the first place the reactionary ethical concept that the physician must wait for the patient to feel sick enough to seek aid has retarded preventive education. Secondly, there is fear that public education in health matters will be misconstrued as "unethical advertising" or that medicine may become less esoteric and mysterious and thereby lose face. Lastly, the vast majority of physicians have been too busy patching up the sick to have time and energy for broad preventive educational activities. However, none of these alibis is valid.

An unenlightened population can not be healthy. It is truly pathetic how few people have more than slight knowledge of how their bodies are put together, how they work, and what their physiological needs, limitations, and capacities are.[30] Education in matters of health, whether it be disseminated in schools, via radio or television, to industrial employees, by books, articles, or by any medium whatever, should be the responsibility and under the direction of physicians who know what is being taught. Oversimplification can be disastrous by fostering overconfidence, self-diagnosis, and self-medication.

Particularly important in the future teaching of hygiene, focused on the prevention of chronic disease in later maturity, is instruction regarding nutrition. Rather than permit the public to get most of its information (or misinformation) from the advertisements of the food industry, it behooves the medical profession to take the initiative in accurate education. Malnutrition includes excesses as well as deficiencies; obesity is a much more significant problem than underweight in this country.[31] As Artemus Ward once said, "Ignorance is not not knowing, it is knowing so many things that ain't so."

In private practice the physicians can do far more in the prevention, retardation, and alleviation of disability that is due to chronic progressive disease in the aging and the aged than is being accomplished at present.[32] Aside from the instruction, guidance, and stimulation of motivation for effort toward the construction of optimum health by personal, tutor-like instruction,[33] the most important potentiality for service is the earliest possible detection of degenerative disease and the institution of measures to correct the known and/or suspected etiological factors. As previously pointed out, these disorders begin so silently and insidiously that they must be searched for if they are to be discovered in time to be amenable to therapy. To wait until obvious symptoms and signs appear is to wait too long. Irreversible damage is the price of procrastination and lack of thoroughness in clinical study. The wholesale approach by multiple screening clinics [26] is valuable, but the mesh of the screen is too coarse. The clinician must be alert for extremely subtle changes suggestive of occult depreciation. Premonitory or predisposing factors to degenerative changes warrant close and detailed attention and correction. For example, dryness of the skin and hair, and perhaps a not unusual bradycardia, should suggest hypothyroidism [21]; obesity and a carefully recorded family history may lead to the anticipation of diabetes mellitus and thus avoid disability; confusion, mild depression, and memory impairment, even if minimal and nondisabling, may be the precursors of arteriosclerotic psychosis and permit of stimulation to activities and correction of anemia and vasodilation therapy, and thus reduce the load of senile psychotics now

28. Footnote 12. Stieglitz.[16b] Stieglitz, E. J.: Constructive Medicine, Science **100**: 313 (Oct. 6) 1944.

29. Mental Disorders in Later Life, edited by O. J. Kaplan, ed. 2, Stanford, Calif., Stanford Univ. Press, to be published.

30. Carlson, A. J.: The Science of Biology and the Future of Man, Science **100**: 437 (Nov. 17) 1944. Stieglitz.[6]

31. Carlson, A. J.: Some Obstacles in the Path Towards Optimum Diet, Science **97**: 385 (April 30) 1943; 412 (May 7) 1943.

32. Footnote 12. Stieglitz.[16b]

33. Stieglitz, E. J.: Aging as an Industrial Health Problem, J. A. M. A. **116**: 1383 (March 29) 1941; The Potentialities of Preventive Geriatrics (Delta Omega lecture), New England J. Med. **225**: 247 (Aug. 14) 1941; Preventive Geriatric Medicine, Journal-Lancet **65**: 60 (Feb.) 1945. Footnote 12.

overcrowding the mental hospitals. These signs of predisposing forces are of the utmost importance.[34] Anticipation is requisite to maximum therapeutic accomplishment. It does not suffice to have only hindsight to explain the pathogenesis of established disease.

Geriatric medicine must be concerned primarily with individuals and their health (functional competence in every capacity) rather than with disease entities. In order that the full potentialities of knowledge may be utilized, geriatric medicine must be anticipatory. It is during early senescence that the most can be accomplished; truly aged or senile persons are the terminal consequences of aging and chronic disease. Anticipatory medicine is more than prevention. Prevention is usually concerned with avoiding specific diseases rather than with improvement of health per se. Anticipatory medicine attempts to construct health, to approach the optimum. The keystone of the arch is the properly conducted, periodic health inventory with wise and pragmatic guidance; the abutments are thoroughness and individualization. Far more can be accomplished by this approach than is generally appreciated.

Anticipatory geriatric medicine does not hope to accomplish miracles. However, if health is maintained during maturity and senescence, the problems of chronic and progressive disablement can be immensely reduced. In the care of those already partially disabled by reason of degenerative disorders, motivation on the part of the patient plays a major role. Improvement in the desire to help oneself reduces invalidism markedly. The things patients can do, not the capacities that have been lost, must be emphasized. Disability is as relative as ability. Requisite is a purpose in living over and beyond mere survival. The primary tragedy of old age or disability due to illness is the awareness of uselessness. Adaptation to handicaps and development of remaining abilities can do much to reverse the trend toward increasing invalidism. Contrariwise, anything that makes disability profitable or desirable (such as compensation and over-solicitude on the part of the family or attendants) perpetuates and enhances invalidism.

SUMMARY

The immensity, complexity, and urgency of the problems of chronic illness in senescence need no reiterative emphasis.[35] Age per se is rarely a major factor in this disablement of the elderly; the accumulative injuries of progressive chronic circulatory and metabolic disorders account for the vast majority of incompetent aging and aged. These degenerative diseases have several generic characteristics that conspicuously modify the problems: (1) multiple, variable, largely endogenous etiology, (2) silent asymptomatic onset, (3) persistent progression, and (4) variability and superimposition of several disorders so that sharply defined entities are exceptional. These disorders can not be prevented by the usual wholesale methods of public health and control of the environment. Individualization in medical care is essential. Equally essential are the initiative and self-discipline of the individual patient.

Health in later maturity can not be given; it must be earned. In chronic illness it is most important not to promise either too little or too much. Morale and the necessary efforts toward rehabilitation are vital factors. Violent reactionary depression follows failure of overly optimistic promises. Not infrequently the maintenance of a status quo in health for a person with progressive illness is a major therapeutic accomplishment. The physician fights delaying actions. We must expect to lose every patient ultimately. Nevertheless, the field is full of challenge and reward. In diseases of senescence the physician deals with subtle, insidious changes, which demand the highest diagnostic acumen for their detection, identification, and evaluation, and the greatest therapeutic skill individually applied. Geriatric medicine is no area for those who are intellectually lazy.

1726 Eye St., N.W.

34. Footnote 3 and 12. Stieglitz.[15] Stieglitz.[16b]

35. Carlson, A. J., and Stieglitz, E. J.: Physiologic Changes in Aging, Ann. Am. Acad. Polit. & Social Sc. **279**: 18 (Jan.) 1952.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

REPORT OF THE COUNCIL

The Council on Physical Medicine and Rehabilitation has authorized publication of the following report.

RALPH E. DE FOREST, M.D., *Secretary.*

F. C. C. RULES FOR DIATHERMY EQUIPMENT MANUFACTURED PRIOR TO JULY 1, 1947

Postponement of Effective Date of Compliance

The effective date for compliance with the rules of the Federal Communications Commission concerning diathermy equipment manufactured prior to July 1, 1947, has been postponed one year, to June 30, 1953.

Physicians or hospitals now using nonconforming short wave diathermy apparatus should replace the equipment with apparatus accepted by the Council on Physical Medicine and Rehabilitation before that date.

On May 9, 1947, the Federal Communications Commission released a public notice assigning three frequencies, in harmonic progression, for medical diathermy and industrial heating equipment.[1] The channels assigned were 13,660, 27,330, and 40,980 kilocycles, corresponding to approximately 22, 11, and 7½ meters wavelength. Later these channels were changed to 13,560 kilocycles plus or minus 6.78 kilocycles, 27,120 kilocycles plus or minus 160 kilocycles, and 40,680 kilocycles plus or minus 20 kilocycles. The Commission ruled that the existing diathermy equipment, provided it did not interfere with radio communication, could be used for a period of five years or until July 1, 1952, before it was declared nonconforming equipment.

On March 14, 1952, the Council on Physical Medicine and Rehabilitation forwarded a petition to the Federal Communications Commission requesting an extension of the deadline to December 31, 1953, or for a period of one and one-half years. The reasons were: (1) that several thousand physicians and hospitals would be in violation of the Rules of the Federal Communications Commission or would have to deprive their patients of the therapeutic benefits of diathermy apparatus, and (2) that the present capacity of the industry to produce ample diathermy appliances is insufficient because of cutbacks of materials and difficulty in obtaining labor.

1. Federal Communications Announces its Regulations for Short Wave Diathermy Apparatus, Report of the Council on Physical Medicine, J. A. M. A. **135**: 30 (Sept. 6) 1947.

Other medically interested organizations supported the petition, as for example, the Physical Therapy Manufacturers' Association, independent manufacturers, the Veterans Administration and other medical groups.

In Public Notice 77631, dated June 26, 1952, the Federal Communications Commission announced that the effective date of the rules for diathermy and industrial heating equipment, the manufacture and assembly of which was completed prior to July 1, 1947, had been extended to June 30, 1953. This period is a one year extension of the deadline.

The present ruling does not change the status of surgical diathermy apparatus, which remains exempt; that is, electrosurgical instruments need not be replaced or discarded in order to comply with the rules of the Federal Communications Commission.

The Commission pointed out that some industrial organizations had objected to the proposed extension on the grounds that the users of medical diathermy equipment had not proceeded diligently to replace nonconforming equipment and that an unconditional extension of the date would invite further procrastination.

The Federal Communications Commission, after careful consideration, declared that a one year extension was in the public's interest and that noncompliance by June 30, 1952, may have been caused, in part, by the nonavailability of accessories and raw materials. In adopting this extension of time the Federal Communications Commission pointed out that failure on the part of the users of medical diathermy equipment to act diligently during the past five year period to replace nonconforming equipment had been a contributing cause to the present inability of manufacturers to meet the demand.

The Commission advises all interested parties that, if further requests for extension of the applicability date are sought, the Commission will give consideration to the advisability of acting on such requests individually.

The Council on Physical Medicine and Rehabilitation appreciates the cordial cooperation of the Federal Communications Commission in extending the date line for complying with its rules relative to medical diathermy apparatus.

APPARATUS ACCEPTED

The following additional product has been accepted as conforming to the rules of the Council on Physical Medicine and Rehabilitation of the American Medical Association for inclusion in Apparatus Accepted. A copy of the rules on which the Council bases its action will be sent on application.

RALPH E. DE FOREST, M.D., *Secretary.*

Kidde Tubal Insufflator, Office Model No. 605700

Kidde Manufacturing Co., Inc., 35 Farrand St., Bloomfield, N. J.

Kidde Tubal Insufflator

Office Model No. 605700 of the Kidde Tubal Insufflator succeeds a previously accepted model. It is an apparatus for the controlled injection of carbon dioxide into the uterine tubes for diagnostic and therapeutic purposes.

Unpacked, the new apparatus measures 40 (height) by 19 by 10 cm. (15¾ by 7½ by 4 in.) and weighs 5.2 kg. (11½ lb.). Packed for shipment it measures 44.5 by 22 by 13 cm. (17½ by 8½ by 5 in.) and weighs 6.4 kg. (14 lb.). The shipping weight includes the weight of one length of manometer tubing, one length of cannula tubing, and three carbon dioxide cartridges.

Practical tests under conditions acceptable to the Council showed that the apparatus was well constructed and worked satisfactorily in the physician's office.

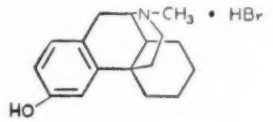
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Methorphinan Hydrobromide.—Dromoran Hydrobromide (Hoffmann-LaRoche).—3-Hydroxy-N-methylmorphinan hydrobromide.—$C_{17}H_{23}NO.HBr$.—M.W. 338.29.—The structural formula for methorphinan hydrobromide may be represented as follows:



Actions and Uses.—Methorphinan hydrobromide is a potent synthetic analgesic related chemically and pharmacologically to morphine. Experimental studies in animals indicate that it is capable of producing the same intensity of analgesia as morphine and with much smaller doses. However, this does not provide a greater margin of safety because the ratio of acute toxicity to analgesic activity in animals is approximately equal for both methorphinan and morphine. In comparable analgetic doses, methorphinan appears to be somewhat longer acting than morphine.

Clinically, methorphinan hydrobromide exhibits the same side-effects and addiction liability as morphine. Some clinical observers report that the drug produces a lesser degree or incidence of undesirable side-reactions than comparable analgetic doses of morphine, but further experience is necessary to establish these observations. When this drug is used, the same precautions should be observed as when other addicting analgesics are used.

Dosage.—Methorphinan hydrobromide is administered parenterally, usually subcutaneously or intramuscularly, unless special circumstances warrant intravenous administration. The hypodermic dose varies from 1 to 5 mg. depending on the age and weight of the patient and the severity of the pain to be controlled.

Tests and Standards.—

Physical Properties: Methorphinan hydrobromide is a fluffy, white, crystalline powder with a bitter taste. It melts between 195 and 197°. It is soluble in alcohol, sparingly soluble in water, slightly soluble in chloroform and very slightly soluble in ether. A 2% solution is clear and practically colorless, and has a pH between 5.0 and 5.6.

Identity Tests: Dissolve about 10 mg. of sodium molybdate in 10 ml. of sulfuric acid. Place about 1 mg. of methorphinan hydrobromide on a spot plate and add 5 drops of the molybdate solution: the solution turns greenish yellow.

Add about 2 drops of 40% formaldehyde to 3 ml. of sulfuric acid. Place about 1 mg. of methorphinan hydrobromide in a spot plate and add 5 drops of the formaldehyde solution: the solution turns brownish yellow. Dilute the solution with about 1 ml. of water: it turns greenish yellow.

Transfer about 50 mg. of methorphinan hydrobromide to a test tube, add about 5 ml. of water and 5 drops of nitric acid. Add 2 ml. of silver nitrate T.S.: a pale yellow precipitate forms, which dissolves slowly in ammonia T.S. *(presence of bromide).*

A 0.005% alcohol solution of methorphinan hydrobromide exhibits ultraviolet absorption maxima at about 2210 Å [E(1%, 1 cm.), about 190] and 2820 Å [E(1%, 1 cm.), about 65] with a minimum at about 2450 Å.

Purity Tests: Dry about 1 gm. of methorphinan hydrobromide, accurately weighed, at 120° for 4 hours: the loss in weight is not more than 3.0%.

Char about 0.5 gm. of methorphinan hydrobromide, accurately weighed. Cool, add about 1 ml. of sulfuric acid and continue ignition until no carbon remains: the amount of residue is not more than 0.1%.

Assay: (Methorphinan) Transfer about 0.2 gm. of methorphinan hydrobromide, accurately weighed, to a separatory funnel and dissolve it in 20 ml. of water. Add 1 gm. of sodium bicarbonate and shake carefully.

Extract the base with eight 25 ml. portions of a 1:3 chloroform-ether mixture and combine the extracts in a 250 ml. separatory funnel. Wash the extracts with three 5 ml. portions of water. Re-extract the wash solution with two 10 ml. portions of chloroform-ether, adding these extracts to the combined chloroform-ether extracts. Add exactly 10 ml. of 0.1 *N* hydrochloric acid to the extract, shake thoroughly for 2 min. and transfer the aqueous layer to an Erlenmeyer flask. Add two 5 ml. portions of water to the chloroform-ether and without shaking transfer the aqueous layer to the acid extract. Wash the chloroform-ether with four 10 ml. portions of water, combining the washings with the acid extract. Titrate the excess acid with 0.1 *N* sodium hydroxide, using 2 drops of methyl red T.S. as an indicator. Each milliliter of 0.1 *N* hydrochloric acid is equivalent to 0.02584 gm. of methorphinan or 0.03383 gm. of methorphinan hydrobromide. The amount of methorphinan hydrobromide present is not less than 98.5 nor more than 101.5%.

Dosage Forms of Methorphinan Hydrobromide

SOLUTION. *Identity Tests:* The solution responds to the identity test for bromide described in the monograph for Methorphinan Hydrobromide.

Evaporate to dryness on a spot plate two portions of the solution containing about 2 mg. of methorphinan hydrobromide. The residues respond to the color identity tests listed in the monograph for Methorphinan Hydrobromide.

Assay: (Methorphinan) Transfer to a separatory funnel an amount, accurately measured, of the solution equivalent to about 50 mg. of methorphinan hydrobromide. Add 5 ml. of 5% sodium carbonate and extract the liberated base with six 20 ml. portions of 1:3 chloroform-ether. Wash the combined extracts with two 5 ml. portions of saturated sodium chloride. Add exactly 10 ml. of 0.02 *N* hydrochloric acid to the extract, shake thoroughly for 2 min. and transfer the aqueous layer to an Erlenmeyer flask. Add two 5 ml. portions of water to the chloroform-ether and, without shaking, transfer the aqueous layer to the acid extract. Wash the chloroform-ether with four 5 ml. portions of water and combine the washings with the acid extract. Titrate the excess acid with 0.02 *N* sodium hydroxide, using 2 drops of methyl red T.S. as an indicator. Each milliliter of 0.02 *N* hydrochloric acid used is equivalent to 0.005167 gm. of methorphinan or 0.006766 gm. of methorphinan hydrobromide. The amount of methorphinan hydrobromide present is not less than 93.0 nor more than 107.0% of the labeled amount.

Hoffmann-LaRoche, Inc., Nutley, N. J.

Solution Dromoran Hydrobromide: 1 cc. ampuls and 10 cc. vials. A solution containing 5 mg. of methorphinan hydrobromide in each cubic centimeter. Ampul solutions are preserved with 0.18% methylparaben and 0.02% propylparaben; vial solutions are preserved with 0.45% phenol. U. S. patent 2,524,855 (Expires October 10, 1967). U. S. trademark 540,115.

Potassic Saline (Darrow).—A mixture of salts available as an aqueous solution containing 0.27% of potassium chloride-U.S.P. (KCl), 0.30% of sodium chloride-U.S.P. (NaCl), and 0.60% of sodium lactate ($CH_3CHOHCOONa$) of quality used in Sodium Lactate Injection-U.S.P.

Actions and Uses.—Potassic saline solution is used parenterally in the treatment of dehydration and acidosis associated with potassium deficiency (particularly that resulting from severe diarrhea). The solution should be employed only when the kidneys are functioning and after initial treatment of shock to ensure adequate circulation. Because of its potassium content and the necessity for caution in administration, potassic saline solution should not be promiscuously employed for restoration of fluids and electrolytes ordinarily replenished with other types of parenteral solutions. Cardiac changes from potassium overdosage may be the only signs of toxicity. Blood potassium determinations and electrocardiographic examinations should be made frequently as precautions against these toxic effects. The blood potassium should be maintained below 20 mg. per 100 cc.

Dosage.—Potassic saline solution is administered by hypodermoclysis when possible; by venoclysis only when necessary. The total daily dose should seldom exceed 80 cc. of the solution (0.216 gm. of potassium chloride) per kilogram of body weight. The rate of administration should be such as to spread the total daily dose over a period of 8 to 12 hours, and administration time over at least four hours. For venoclysis in the treatment of severe infant dehydration and diarrhea, dilution of potassic saline solution with one to two parts of a 5% dextrose solution by simultaneous administration via Y-tube connection is advised. Initial treatment of shock with blood or plasma in severely ill patients, or with other parenteral fluids in milder cases, is essential.

For accidental potassium poisoning, 10% of calcium gluconate sufficient to counteract the inhibitory cardiac effect of potassium should be slowly administered by intravenous injection.

Tests and Standards.—

POTASSIUM CHLORIDE. The potassium chloride used in the preparation of potassic saline (Darrow) responds to the description and standards in the U.S.P.

SODIUM CHLORIDE. The sodium chloride used in the preparation of potassic saline (Darrow) responds to the description and standards in the U.S.P.

SODIUM LACTATE. The sodium lactate used in the preparation of potassic saline (Darrow) is of the quality required for Sodium Lactate Injection-U.S.P.

Dosage Forms of Potassic Saline (Darrow)

SOLUTION. *Physical Properties:* Potassic saline solution (Darrow) is a clear, colorless liquid with a pH between 6.70 and 6.90.

Identity Tests: Pick up some potassic saline solution (Darrow) on a loop of platinum wire moistened with diluted hydrochloric acid and heat it in a colorless flame: the flame becomes bright yellow *(presence of sodium)*. Repeat the test and view the flame through a cobalt glass: the flame becomes violet *(presence of potassium)*.

To 1 ml. of solution add several drops of diluted nitric acid and 1 ml. of silver nitrate T.S.: a white precipitate forms which is soluble in excess diluted ammonia solution *(presence of chloride)*.

To 5 ml. of the solution add 2 drops of sulfuric acid and 5 ml. of potassium permanganate T.S., and warm the solution: the odor of acetaldehyde becomes noticeable *(presence of lactate)*.

Purity Tests: With 20 ml. of potassic saline solution (Darrow) and omitting the treatment with sulfuric and sulfurous acids, run a comparative test for arsenic as directed in *U.S.P. XIV*, p. 684: the arsenic limit is 0.1 ppm.

To 20 ml. of potassic saline solution (Darrow) add 2 ml. of diluted hydrochloric acid and dilute to 25 ml. with water: the heavy metals limit, *U.S.P. XIV*, p. 717, is 0.3 ppm.

Assay: (Potassium Chloride) Pipet 10 ml. of potassic saline solution (Darrow) into a porcelain dish and add 5 ml. of 10% chloroplatinic acid. Evaporate on a steam bath nearly, but not quite, to dryness, that is, to a point where the contents of the dish will solidify on cooling. Add 3 ml. of alcohol and break up the crystalline mass into a fine powder with a glass rod. Decant the alcohol through a tared fritted glass crucible with a minimum of transference of the solid into the crucible. Repeat the washing 8 to 10 times using 1 ml. portions of alcohol, grinding the powder each time, and decanting the alcohol through the crucible until the filtrate is colorless and the crystals of potassium chloroplatinate in the porcelain dish are golden yellow and no longer tinged with orange. Dry the crystals in the dish over a steam bath for several minutes. Transfer as much as possible of the dried crystals from the dish to the crucible and wash the remaining crystals into the crucible with a minimum amount of alcohol. Dry the crystals for 0.5 hour at 105° and weigh. Each milligram of potassium chloroplatinate formed is equivalent to 0.3068 mg. of potassium chloride. The amount of potassium chloride present is not less than 95.0 nor more than 105.0% of the labeled amount.

(Sodium Chloride) Pipet 25 ml. of potassic saline solution (Darrow) into a glass-stoppered Erlenmeyer flask. Add 50 ml. of water, 50 ml. of 0.1 *N* silver nitrate, 3 ml. of nitric acid and 3 ml. of nitrobenzene. Swirl the contents of the flask to entrap the precipitate, add 2 ml. of ferric ammonium sulfate T.S., and titrate the excess silver nitrate with 0.1 *N* ammonium thiocyanate. Each ml. of 0.1 *N* silver nitrate consumed is equivalent to 3.546 mg. of total chloride. To calculate the amount of sodium chloride present, (1) multiply the number of mg. in 100 ml. as obtained in the potassium chloride assay by 0.4756 to obtain the amount of chloride present as potassium chloride. (2) Subtract this amount from the number of mg. of chloride per 100 ml. found in the total chloride assay and multiply the difference by 1.649 to obtain the number of mg. of sodium chloride present in 100 ml. of solution. The amount of sodium chloride present is not less than 95.0 nor more than 105.0% of the labeled amount.

(Sodium Lactate) Pipet 100 ml. of potassic saline solution (Darrow) into a platinum dish and evaporate it to dryness. Dry the residue at 105° for at least 24 hours. Carefully heat the dish until the mass is thoroughly charred. Pulverize the charred mass with a glass rod, add 25 ml. of water and 75 ml. of 0.1 *N* sulfuric acid. Heat the dish on a steam bath for 0.5 hour and with a glass rod break up any lumps which may form. Filter, wash the precipitate with hot water until the filtrate is neutral to litmus, cool the combined filtrate and washings, and titrate the excess acid with 0.1 *N* sodium hydroxide using methyl red T.S. as an indicator. Each milliliter of 0.1 *N* sulfuric acid is equivalent to 11.20 mg. of sodium lactate. The amount of sodium lactate present is not less than 95.0 nor more than 105.0% of the labeled amount.

Don Baxter, Inc., Glendale, Calif.

Solution Potassic Saline (Darrow): 500 cc. Vacoliter bottles. A solution containing 2.7 mg. of potassium chloride, 3 mg. of sodium chloride, and 6 mg. of sodium lactate in each cubic centimeter.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
535 N. DEARBORN ST. . . . . CHICAGO 10, ILL.
Edited by . . . . . AUSTIN SMITH, M.D.
Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
Editor for Medical Literature Abstracts . GEORGE HALPERIN, M.D.

Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

FOCAL INFECTION

After exerting a tremendous influence on the practice of medicine for a generation, the theory of focal infection in the past 10 or 15 years has fallen in part into disfavor. This has been due partly to the excesses and abuses that have been committed in its name and partly to the following observations that seem to discredit it. 1. Many patients with diseases presumably caused by foci of infection have not been relieved of their symptoms by removal of the foci. 2. Many patients with these same systemic diseases have no evident focus of infection. 3. Foci of infection are, according to some statistical studies, as common in apparently healthy persons as in those with disease.

The observations just cited appear damning, but, as Kolmer,[1] Kern,[2] Irons,[3] and others have pointed out, none of them actually disproves the theory that some foci of infection can in the presence of predisposing or accessory factors produce some systemic diseases. A focus of infection can be compared to a lighted match that has started a forest fire. Just as the extinguishing of the match does not put out the forest fire or repair the damage done to the trees, so the removal of the focus of infection may not eliminate the disease it initiated or reverse permanent tissue changes. This does not prove, however, that the focus did not initiate the disease, or that earlier removal of the focus might not have prevented advance of the disease. Likewise, failure of removal of a single focus to affect the progress of a disease does not prove that other undiscovered foci are not responsible for its maintenance. Similarly, the failure to find foci in some patients with diseases commonly attributed to foci does not prove the absence of concealed foci or the absence of foci at the time of initiation of the disease. Also, it does not prove that a mechanism similar to that of focal infection is not operative in these cases, as when bacteria present on the surface of the oral, respiratory, gastrointestinal, or genitourinary mucous membranes penetrate these natural barriers, following physical trauma, chemical irritation, or vascular disturbances, and produce a temporary bacteremia. Finally, the fact that foci of infection are present in many persons without systemic disease does not prove that foci are incapable of producing disease. It only proves that foci alone, without accessory factors, such as trauma, circulatory disturbances, or alterations in immunity are not sufficient to produce secondary disease. Thus on logical grounds alone the basic theory cannot be discarded.

In positive support of a modified theory of focal infection is the fact that certain foci are known to be capable of producing disseminated disease. Kolmer supplies a long list of such foci and diseases in an extensive review.[1] A cutaneous abscess for instance may, if subjected to trauma, give rise to bacteremia resulting, in susceptible patients, in acute bacterial endocarditis, osteomyelitis, suppurative arthritis, perirenal abscess, or a variety of other systemic manifestations. Dental foci of infection have been observed to give rise to transitory bacteremia following mastication or massage of the gums, and extraction of teeth infected with Streptococcus viridans has resulted in the development of subacute bacterial endocarditis due to the same organism. Bacteremia has also been detected following massage of an infected prostate, and there is no reason to believe that it may not occur as a result of the stress applied to infected tonsils or other compressible foci of infection during contraction of adjacent muscles. Localized infections with Corynebacterium diphtheriae, Clostridium tetanus, and hemolytic streptococci produce distant effects such as myocarditis, muscle rigidity, or a scarlatiniform eruption by means of toxins liberated by the organisms. Similar but less dramatic effects are possible in focal infections due to other organisms liberating exotoxins. Local infection of the throat with group A beta-hemolytic streptococci is sometimes followed in susceptible persons by acute rheumatic fever. This is presumably the result of sensitization of the connective tissues of the joints and heart to the organisms disseminated from the focus or to the products of their interaction with the tissues of the host. Chemotherapeutic and antibiotic prophylaxis of respiratory infections has been demonstrated to reduce the incidence of rheumatic fever. These examples in conjunction with others cited by Kolmer lead him to conclude that the etiological role of focal infection in some systemic diseases is no longer theory, but fact. Collateral evidence is supplied by the observation that relief of symptoms follows removal of foci in some patients with early disease.

The fact that some foci participate in the production of some diseases does not, however, justify the assumption that all foci produce disease or that all poorly understood diseases are due to foci of infection. The causative role of foci in such diseases as rheumatoid arthritis has been neither proved nor disproved. While it is theoretically possible that this disease originates as an allergic reaction to bacteria or their products, direct proof is lacking. In any case it is well established that removal of foci in patients with advanced rheumatoid arthritis is not a curative procedure.

In view of the demonstrated importance of foci of infection in some diseases and the still valid theoretical possibility that they contribute to the production of others, it is apparent that focal infection cannot be ignored in the practice of medicine. On the other hand, the indiscriminate removal of all suspected or potential foci from a person without complaints is to be condemned. An approach to the problem has been suggested by

1. Kolmer, J. A.: Focal Infection in Relation to Health and Disease, J. Am. Dent. A. **45**: 139 (Aug.) 1952.
2. Kern, R. A.: Symposium on Infectious Diseases: What is Left of the Theory of Focal Infection, M. Clin. North America **34**: 1705 (Nov.) 1950.
3. Irons, E. E.: The Theory of Focal Infection: Its Influence on the Practice of Medicine, Proc. Inst. Med. Chicago **16**: 265 (Dec. 15) 1946.

Kolmer [1] and by Kern.[2] In patients with diseases known to be due to focal infection, Kolmer suggests that the primary focus should be eradicated promptly by chemical and/or surgical treatment and that the secondary disease, if due to active infection, should be treated similarly. In early disease, eradication of foci may relieve symptoms; in advanced disease it should not be expected to do so, although it may lighten the load on the body's adaptive capacities. In patients with diseases probably not caused by focal infection, Kern advises that any active foci present should still be removed if they appear to affect unfavorably the general health of the patient. It should be understood by both patient and physician that this removal will not influence the disease directly. Both authors feel that in healthy persons an active focus of infection should be treated not only to eliminate the remote chance that it will produce trouble at a distant site but to remove an abnormality. In Kern's words, "An empty house is better than a bad tenant." The prevention of secondary disease in susceptible persons is even more important than a direct attack on an infected focus. The administration of antibiotics or sulfonamides to patients with rheumatic heart disease during seasons when respiratory infections are prevalent is now accepted practice for the prevention of recurrent attacks of rheumatic carditis, as is the use of these drugs in patients with valvular or congenital heart disease to prevent bacteremia during and after removal of infected teeth or tonsils.

TRAFFIC ACCIDENTS

The National Safety Council has anounced that during the first seven months of 1952 there were 20,000 deaths caused by automobiles. This is an increase of 2% over 1951. Rural accidents were responsible for the rise in fatalities, as cities as a whole experienced a 6% decline. Chicago, however, did not have the same experience as other large cities; it showed the worst record of the five cities with a population of more than a million. And yet, as has been shown repeatedly, traffic accidents can be reduced. In Los Angeles traffic deaths have been cut in half in the last four years, and in Detroit there has been a decrease of 46%, in spite of an increase of 32% in car registrations. This appalling death rate offers more than a statistic to the medical profession. It poses an unusual challenge.

Fatal automobile accidents are now a major cause of death. Bad roads, rain, fog, snow, vehicle defects, and obscured vision are just a few of the causes. However, according to M. Martyn Kafka, one of the most important factors is the condition of the driver. Of course, if he is under the influence of alcohol his condition is usually obvious. Not so obvious may be the effects of drugs, particularly sedatives and stimulants. Also of importance are various diseases, and it has been suggested that a patient's history should include information on whether he drives an automobile and whether he has a disease that might suggest the need for a warning to drive carefully or not at all. Worthy of consideration are advanced heart disease, arteriosclerosis, hypertension, gross visual deficiencies, and lesions of the nervous system. Sometimes less apparent factors are involved in the causation of accidents, for example, degenerative changes in the eyes, color vision disturbances, and loss of depth perception. It has been suggested that patients with these signs of physical defects should be advised that it may be dangerous for them to drive automobiles. In this respect the family physician can assume an important role in the prevention of traffic accidents. By his actions he may save his patient's life and the lives of others. If it were possible to examine periodically all drivers the accident rate undoubtedly would be lowered. Since this is not yet a feasible procedure physicians can make the most of their opportunities when they examine patients for other reasons.

Another factor to be considered is the "mental makeup," "constitutional behavior," or, as some irritated drivers would say, "the sheer cussedness" of those who persist in driving on the wrong side of the road, straddling white lines, and otherwise ignoring even the simplest safety directions. One cannot but wonder at times what such drivers think about—if they think at all. Or, is the fault purely physical and not readily apparent without close examination?

Recently there have been references to "accident prone" persons. The fact that they repeatedly are involved in accidents as drivers and as pedestrians cannot be shrugged off simply as "bad luck." Studies are now in progress to determine what mental or physical characteristics make these persons so liable to accidents.

N. L. Burnette has reported [1] on the need for approaching a phase of traffic accident investigation that might reveal a relation between accident and behavior, injury and emotion. He observed, for example, how consistent driver behavior has been over the years. In 1935, 15% of persons in driving accidents in the United States had been on the wrong side of the road; 17% had simply driven off the road. In 1948, in Ontario the percentages for these errors in driving were approximately 19 and 19 respectively. Burnette stated: "The question posed by these accidents illustrates the difference between a statistic and an epidemiology. The first merely is a tabulation of end results by frequency and distribution. The second would show the relationship of each occurrence to the state of the individual involved." Among the research studies he proposed were those for determination of right or left eye dominance and degrees of discomfort caused by chronic ailments. As he pointed out, "Laymen cannot be expected to realize the connection between impaired health and the risk of accidents, unless people in authority can show them the reasonableness of this. . . . There would need to be enough data to impress the motoring public with the fact that despite the very best intentions to be careful, cautious and law-abiding, a driver can invite mishap if he is not in control of his bodily functions."

In 1951 the Travelers Insurance Companies, Hartford, Conn., reissued a booklet in the interest of street and highway safety that contains data that should cause anyone to ponder over the seriousness of traffic accidents. In 1950, almost 50% of the actions of drivers resulting in deaths were concerned with exceeding the speed limit, 18% with being on the wrong side of the

1. Burnette, N. L.: Traffic Accident Investigation—The Next Phase, Canad. J. Pub. Health 41: 452 (Nov.) 1950.

road, 5% with driving off the roadway. Of the drivers in fatal accidents 24% were in the age group from 18 to 24 years, and 68% in the group from 25 to 64 years. Ninety-eight per cent had driving experience of one year or more. Three out of four traffic accidents occurred in clear weather on dry roads. Almost 78% of the motor vehicles involved in accidents were passenger cars, and 82% of the cars were going straight, not turning left or right or backing. Furthermore, 94% of the cars were in apparently good condition. The most dangerous single hour of the day or night for deaths seemed to be from 6 to 7 p. m.

A combining of such data shows that the 1950 typical accident situation was as follows: The victim was a middle-aged man with several years' driving experience. His passenger car was in apparently good condition, and he was on a straight, dry stretch of open highway. It was 7:30 on a clear Saturday night. He was speeding. He was killed in a collision with another car.

Obviously there is need for increased interest in the cause and prevention of accidents. The medical profession cannot confine itself to merely providing the best treatment available for the injured. Accident prevention today must be included in so-called preventive medicine, and this can best be pursued through careful studies of the causes of accidents and the careful examination of patients known to drive cars. Patients expect wise counsel from their physician when they present themselves because of a complaint. This counsel today must be extended beyond what the patient has usually been led to expect. If his life or the lives of others can be saved by a warning from his physician of the hazards of driving because of certain physical or mental findings he will be experiencing an extension of medical care that is in keeping with the demands of modern life.

MORTALITY REDUCTIONS DURING A HALF CENTURY

Elsewhere in this issue (page 510) is a summary of Bulletin 92, "Mortality Trends in the United States, 1900-1949," recently published by the Bureau of Medical Economic Research of the American Medical Association.[1] Although the emphasis of the bulletin is on causes of death, the numerous charts and tables combined with the penetrating analysis of mortality trends provide physicians and other students of vital statistics with a clear-cut analysis of the spectacular reductions in mortality during the past half century. The decline in the general mortality rate from 17.2 (deaths per thousand) in 1900 to only 9.6 in 1950 is only the starting point for their analysis. A small portion of the 20 year increase in life expectancy at birth resulted from mortality gains at the higher ages; for example, the 22% drop in mortality at ages 65 to 74 accounted for 2% of the increase. The restricted meaning of life expectancy at birth, a term frequently misused by persons who like to make forecasts, is explained and illustrated. Although life expectancy at most ages in Sweden is probably still above the corresponding values for persons in the United States, it does not follow that the people of Sweden, age for age, are destined to live longer than their counterparts in the United States. Life expectancy at any age reflects the mortality rates among older persons in a particular calendar year. What those mortality rates will be 10 or 20 years from now cannot be discerned from any current table of life expectancy values. If the rapid rate of health progress in the United States since 1900 should be continued, our people may have longer lives than the people of any other nation.

Although the mortality rate from all causes combined has declined for every age group since 1900, the number of deaths per thousand population from heart diseases has increased for all age groups over 35, from cancer for every age group, and from diabetes for age groups over 45. Some of these increases are the result of improved diagnoses of the causes of death and changes in record-keeping. Many deaths in 1900 that would have been attributed to ill-defined causes would, under present-day procedures, have been attributed to heart diseases, cancer, or diabetes. The authors doubt that all of the increases in the age-specific rates from heart diseases, cancer, and diabetes should be attributed to these factors. They discuss the possibility that medical progress, by prolonging many impaired lives to the higher ages, may have been responsible, at least in part, for these contra-trends. The records in the United States on morbidity are so poor that no conclusion was reached on this question of impaired lives.

The authors point out again that although heart diseases account for more than five times as many deaths as accidents and twice as many life years lost, nevertheless fatal accidents in 1948, as in 1945 and in 1940, cut off more years from the working lifetimes of the American people than any major cause of death. Accident prevention lags far behind medical progress.

In this century the average age at death from each of the major causes of death has risen. The seven leading causes now account for three-fourths of our deaths, as compared with only one-half in 1900. Perhaps this fact accounts for some of the trend toward specialization in medicine. For the physician attending a patient in his final illness today is likely to be treating him for heart disease or cancer, whereas in 1900 it might have been any of a much larger number of diseases.

The authors of Bulletin 92 suggest that henceforth the National Office of Vital Statistics cease to publish the maternal mortality rates, because the current rates are so very low and the problems are now local whereas they were formerly national. For similar reasons they also suggest that the traditional infant mortality rate be no longer computed and published but that the neonatal rate (for the first month of life) be substituted. By these two suggestions the authors emphasize their belief that an era has ended. They conclude that it has been "man's greatest half century."

We started the 20th century with many health disadvantages. The record of accomplishment set forth in Bulletin 92 provides the basic reason why physicians and other enlightened citizens should hold fast against any and all schemes to destroy our system of medical care under which this astounding record was made.

1. A copy of Bulletin 92, by Frank G. Dickinson, Ph.D., and Everett L. Welker, Ph.D., may be obtained by writing to the Bureau of Medical Economic Research, American Medical Association, 535 N. Dearborn St., Chicago 10.

ORGANIZATION SECTION

PARTICIPATION IN ELECTION CAMPAIGNS

The American Medical Association has received many requests from physicians for information concerning individual and collective participation in political campaigns. Many physicians wish to assume active roles in the election of candidates they prefer, but have hesitated to do so for fear of innocently violating provisions of the federal election laws. To help clarify this situation, the most important federal laws and regulations pertaining to an individual's or an organization's participation in election campaigns are hereby summarized.

This condensed version is based on a detailed interpretation by the law firm of Kirkland, Fleming, Green, Martin and Ellis, Chicago. Inasmuch as this summary concerns only federal laws and a state may have additional election laws, it is suggested that the individual physician or organization ascertain whether additional election laws exist in their state, and, if so, that they become familiar with them before proceeding with political activity. Certain sections of the laws and regulations are ambiguous and conflicting and can only be adjudicated by court procedure.

Federal Election Laws and Regulations Regarding Persons Not Employed by Government Agencies

It is the right and duty of every citizen aggressively to further the candidacy of any qualified candidate for federal office and to oppose actively the candidacy of anyone he feels to be unqualified. All citizens, including any individual member of the medical profession, may freely and extensively engage in political activities, contribute and expend funds, make speeches, distribute pamphlets, and engage in electioneering for or against any party or candidate except as specifically prohibited in the manners described below. The regulations below do not include those specifically designed for government employees.

Financial Contributions.—No person can give, directly or indirectly during any one calendar year, more than $5,000 in connection with a nomination or election to federal office, to or on behalf of any candidate, committee, or organization engaged in furthering the nomination or election of any candidate to federal office, or to the success of any national political party. This does not apply to contributions made to state or local committees that are not branches of national committees. There is no federal limit on contributions made to these state or local committees.

When an expenditure of $50 or more is made in two or more states in any one year for a candidate for the house or senate in a general election, the person making the expenditure must report such transactions to the Clerk of the House of Representatives. Such expenditures made in behalf of a presidential candidate or to a political committee need not be reported, however.

No one can purchase goods, commodities, or advertising the proceeds from which can be put to use to the benefit of a candidate for federal office or of any national political committee.

A detailed account of all contributions received by a person for a political committee must be rendered to the treasurer of the committee within five days after receipt. This information should include the name and address of the contributor and the date received.

Threats and Bribes.—An individual is prohibited from coercing, intimidating, or threatening anyone in connection with his right to vote or not to vote as he chooses for any candidate. Included in this section is the offer of money by one person to another for voting a certain way or for withholding his vote. Individuals are also prohibited from accepting, soliciting, or receiving any such expenditure in consideration of his vote. No one can promise or withhold a federal job or other federal benefit to anyone as a reward or as punishment for political activity in support of or in opposition to any candidate or political party.

Literature.—No person can publish or distribute any printed material relating to or concerning any candidate without disclosing in it the name of the party and the officers responsible for such publication. In addition, printed material reflecting injuriously on the character or conduct of a candidate on the outside cover or envelope may not be mailed or delivered.

Federal Election Laws and Regulations Regarding Persons Employed by Government Agencies

Many individual physicians are associated in a professional capacity and otherwise with agencies of the government and with federally supported state and local agencies. All persons who receive compensation from federal, state, city, or local government agencies for services rendered, whether it be on a full-time, part-time, or per diem basis, are considered government employees. Excluded from this category are officers and employees of the legislative and judicial branches, persons who are retained on a fee basis to perform a special service and who take no oath of office, those receiving benefit payments, the President and Vice-President, presidential appointees subject to Senate confirmation, and persons paid from the appropriation for the office of the President. Officers and employees of any educational institution, research institution, or system supported wholly or partially by state, county, city, religious, or charitable funds are excluded from federal regulations that prohibit their using their official authority or position to influence elections and taking an active part in political management and political campaigns. In addition to the regulations cited for the individual citizen, the following laws are applicable to persons employed by governmental agencies.

Threats and Bribes.—No person who receives compensation from the United States Treasury can discharge, promote, or threaten to degrade or change the official rank or compensation of any federal employee for giving, withholding, or neglecting to give a contribution for any political purpose. No person in the service of the United States can give any other person in the service any money on account of or to be applied to the promotion of any political object.

Influencing Votes.—No person who is an employee in any agency or department of the executive branch of the federal government can use his official authority or influence for the purpose of influencing or interfering with an election. He cannot take an active part in any political management or campaign, even though he still retains his right to vote or to express his opinion on political subjects.

Any officer or employee of any state or local agency thereof, whose principal employment is connected with any activity financed wholly or partially by United States government loans or grants, is prohibited from using his official authority or influence to interfere with an election or nomination for federal office. He may not directly or indirectly coerce or advise any other such officer or employee to contribute anything of value to any party or committee for political purposes, and he may not take an active part in any political management or campaign. Principal employment has been found to mean principal public employment, regardless of whether a person works only occasionally for an affected agency. Comparative time spent in private or self-employment is not considered in determining a person's principal public employment.

Soliciting.—No person can solicit or receive any contribution in any federal building, Navy yard, fort, or arsenal.

Contract Employees.—No person entering into a contract with any department or agency of the United States where payment

for services is to be made in whole or part from federal funds can contribute or make a promise of contribution to any political party, federal candidate, or any person for political purpose or use during the period of negotiation or lifetime of the contract.

Federal Election Laws and Regulations Regarding Organizations

Corporations, national banks, and labor unions, organized for profit or not for profit, or officers thereof, are not permitted to make any contribution or expenditure of any kind whatsoever for or in connection with any election to any federal office, to any primary or political convention, or to any caucus held to select candidates for any federal office. No person is permitted to accept or receive any such contribution from any of the above-mentioned groups. This ruling includes the expenditure of funds for the purchase of advertising or radio time in connection with any federal election.

Any periodical, magazine, or newsletter published and circulated by any corporation to its members or stockholders in the regular course of its business may discuss, attack, or favor pending or proposed legislation. However, if such a publication desires to oppose or support any candidate for federal office, it is suggested that the entire cost be paid for from funds derived solely from members' or stockholders' individual subscriptions and from proceeds of advertising usually appearing therein. This is to avoid any possibility of charges that the corporate funds were being expended in connection with an election. Distribution of these publications should be confined to members and stockholders, and no special editions or pamphlets should be printed or distributed, even to members or stockholders. All corporations and other organizations, whether partnerships, committees other than political, associations, or other groups of persons, are subject to the same prohibitions and penalties which apply to individuals.

Political Committees

Any group of citizens, whether on a national, state, or county level, can, as individuals, form political action committees. Congress has recognized the existence of purely political committees in connection with federal elections and has prescribed detailed regulations in regard to such committees that operate in two or more states or that are branches or subsidiaries of a national political committee, association, or organization.

The law defines a political committee as any committee, association, or organization that accepts contributions or makes expenditures for the purpose of influencing or attempting to influence the election of candidates or presidential and vice-presidential electors (1) in two or more states or (2) whether or not in more than one state, if such committee, association, or organization (other than a duly organized state or local committee of a political party) is a branch or subsidiary of a national committee, association, or organization. Following are regulations that apply to such committees.

Funds.—No political committee shall receive contributions or make expenditures aggregating more than $3,000,000 during any calendar year.

Officials and Duties.—Every political committee shall have a chairman and treasurer and may not function until such officers are appointed. The treasurer must file with the Clerk of the House of Representatives, at stated intervals, detailed statements of all contributions made to or for such committee, the name and address of every person making any such contribution and the date thereof, all expenditures made by the committee, the name and address of every person to whom any such expenditure is made and the date of expenditure, and the total sum of all expenditures made during year.

Restrictions.—Persons forming political committees must not make use of any official position or office that they may hold or occupy in any organization. They must act only as individual citizens. No person who is partially or wholly compensated from federal funds should become a member of any political committee.

A political committee must exist and function independently of all other organizations or corporations. It should not occupy quarters in any property owned by a corporation without paying reasonable rent; clerical help or other assistance should not be supplied by a corporation; and public relations assistance, aid, or information should not be sought or requested by the committee from a corporation's public relations counsel.

WHITAKER AND BAXTER RESIGN A. M. A. ASSIGNMENT

A. M. A. President Louis H. Bauer announced Sept. 22 that Dr. Elmer L. Henderson, Louisville, Kentucky, chairman of the A. M. A. Coordinating Committee, and Clem Whitaker and Leone Baxter, directors of the A. M. A. National Education Campaign, have resigned their A. M. A. assignments.

Dr. Henderson, a past president of the American Medical Association, and two other A. M. A. past presidents, Dr. Ernest E. Irons, Chicago, and Dr. John W. Cline, San Francisco, have accepted leadership in a new Eisenhower-Nixon organization.

This organization, known as a National Professional Committee for Eisenhower and Nixon, will seek to enlist thousands of physicians, dentists, lawyers, engineers, accountants, pharmacists, and other professional men and women in an aggressive, bipartisan drive for the election of the Republican nominees for President and Vice-President. Dr. Henderson will serve as chairman of the committee, and Drs. Irons and Cline will serve as vice-chairmen.

Dr. Henderson has served as chairman of the Coordinating Committee since its creation in January, 1949, to supervise American medicine's nationwide campaign of public education against compulsory health insurance. Whitaker and Baxter have served as managing directors of the campaign since its inception.

"The A. M. A., as a nonpartisan, professional organization, is barred, both ethically and legally, from participating in election campaigns, which explains the action of Dr. Henderson and Mr. Whitaker and Miss Baxter in asking for their release from A. M. A. duties," Dr. Bauer said, adding: "The Association will take no part in the presidential election, except to join with other nonpartisan groups in urging all eligible voters to cast their ballots on election day, regardless of their affiliations or preferences. Individual doctors, of course, are entirely free to engage in election activities and, in fact, have a very real responsibility to make their influence felt for good government."

Vice-chairmen representing other professions on the National Professional Committee for Eisenhower and Nixon include Harold J. Gallagher, New York, past president of the American Bar Association; Dr. Clyde E. Minges, Rocky Mount, N. C., past president of the American Dental Association; Robert Lincoln McNeil, Philadelphia, past president of the American Pharmaceutical Manufacturers' Association; Sidney L. Stolte, St. Paul, Minn., past president of the National Society of Professional Engineers, and John F. Forbes, San Francisco, past president of the American Institute of Accountants. Mr. Whitaker and Miss Baxter will serve as campaign directors of the Eisenhower-Nixon professional committee's drive. The committee's national headquarters will be at 1 North La Salle St., Chicago.

LOCAL ARRANGEMENTS FOR ANNUAL SESSION

Dr. J. Stanley Kenney, 924 West End Ave., New York City, immediate past president of the New York State Medical Society and long active as a member of the A. M. A. House of Delegates, has been appointed by the A. M. A. Board of Trustees as chairman in charge of local arrangements for the annual A. M. A. session, which will be held in New York, June 1-5, 1953.

A. M. A. PRESIDENT REPLIES TO PRESIDENT TRUMAN

On Sept. 25 the Associated Press wire carried the following statement:

"President Truman said today he thought his Philadelphia speech on medical care for the American people, rather than an American Medical Association victory, caused the AMA to disband its group set up to fight his national health program.

"The President commented after he was told at a news conference that the AMA was disbanding its special committee opposed to the Truman health plan on the ground that it was no longer necessary.

"Truman said he thought what finished the battle was a certain speech the President made at Philadelphia. He asserted the AMA officials admit now by their action that they have been wrong.

"The President answered affirmatively when he was asked if he referred to his suggestion that opponents of his plan had not come up with a substitute proposal that would accomplish his goal of making medical aid available to everybody. The President said he did."

Dr. Louis H. Bauer, Hempstead, N. Y., President of the American Medical Association, issued the following statement in reply to Mr. Truman's comments regarding the A. M. A.'s fight against socialized medicine:

"The American Medical Association will never cease its fight against national compulsory health insurance. Mr. Truman's Philadelphia speech had no bearing whatsoever on the decision to disband a special committee set up to conduct an intensive short-term, educational program against socialized medicine. This decision was reached by the A. M. A. House of Delegates last June, and was widely publicized at the time.

"The National Education Campaign was merely one intensive phase in the medical profession's long-range effort to keep medical care on a voluntary basis. This effort will continue as long as attempts are made to shackle the people's health in bureaucratic red tape.

"Mr. Truman is naïve indeed if he believes that any speech he delivers could change the medical profession's basic beliefs concerning high quality medical care."

MEDICAL PR INSTITUTE IN CHICAGO

State and county medical society public relations personnel and interested physicians met Sept. 4-5 at Chicago's Edgewater Beach Hotel for the American Medical Association's first Medical Public Relations Institute. More than 200 representatives from 41 states, Hawaii, and Canada exchanged suggestions on ways of improving the profession's relations with the public.

On the agenda were panel discussions on practical ways to increase physician participation in society activities; whether the code of ethics should be modernized to bring about better relations between mass media and the medical profession; ways of developing the best working relation between the medical profession and the press, radio, and television; tips to the profession on working with community groups, and strengthening medical society public service activities.

At one session devoted to the question of modernizing the Principles of Medical Ethics in order to bring about better relations between the profession and mass media, John L. Bach, director of A. M. A. press relations, gave the viewpoint of medical public relations (press); Arthur Snider, science writer for the *Chicago Daily News*, the viewpoint of the working press; Paul L. Wermer, M.D., Secretary, Committee on Research, the viewpoint of the medical profession, and W. W. Bauer, M.D., Director of the Bureau of Health Education, the viewpoint of medical public relations (radio-television).

Speaking on "What Is Community Relations?", Fred R. Jolly, manager of the community relations for the Caterpillar Tractor Co. of Peoria, Ill., opened the session devoted to the county medical society's place in community affairs. Tips on working with voluntary health agencies, other professions, labor and farm groups, schools and Parent-Teacher Associations, women's clubs, service clubs, and veterans' groups were offered by medical society representatives. Speakers included Robert Richards, executive assistant, Medical Society of the State of Pennsylvania; Arthur P. Tiernan, executive secretary, Vanderburgh (Ind.) County Medical Society; Carl T. Weber, executive secretary, County of Monroe (N. Y.) Medical Society; Aubrey Gates, Field Director, Council on Rural Health; Hart F. Page, assistant director of public relations, Ohio State Medical Society; Mrs. Shelley Davis, Woman's Auxiliary to the Medical Association of Georgia, and William H. Bartleson, executive secretary, Jackson County (Mo.) Medical Society.

On Friday afternoon were clinics on field service, radio and television programing and newsletter editing, and direct mail techniques. Discussion leaders included Glenn Gillette, associate director of public relations, California Medical Association; Frank Baker, radio and television director of Reincke, Meyer and Finn of Chicago, and Charles R. Jordan, president, Jordan-Sieber and Associates, Chicago. Public relations experts from other fields participated in addition to the 25 medical society executives and physicians on the program.

Fourteen state and county societies exhibited in the Project Parade, a visual idea exchange, held in connection with the institute. In the exhibit were displays of printed materials, pamphlets, and photographs of events in which the various societies participated during the past year.

A one-day Medical Public Relations Conference will be held Dec. 1 in Denver, preceding the A. M. A.'s Clinical Session.

CONFERENCE ON MEDICAL CARE IN MINE AREAS

The American Medical Association was well represented at the recent Charleston Conference on Medical Care in the Bituminous Coal Mine area, where state medical societies from Kentucky, Pennsylvania, Tennessee, Virginia, and West Virginia were in attendance. The conference was called by the subcommittee on medical care of industrial workers of the A. M. A. Council on Medical Service to discuss the results of an investigation by a survey team into the extent and types of medical-hospital problems in mining areas. Also in attendance were representatives of the state departments of health, medical schools, and medical administrators of the United Mine Workers' medical service program.

The survey, made in cooperation with the state medical societies, was completed in May, 1952. The conference discussed the mine workers' health program and outlined improvements that should be made. It was the concensus that in some areas new or improved hospital facilities or health centers would be desirable but that in any construction program contemplated by the U. M. W. the needs of the entire community must be kept in mind. It also was felt that improved living and professional working conditions should be provided in certain regions in order to attract the physicians who are needed. Mine workers, it was decided, should be given more information concerning the prevention of diseases and accidents and a better knowledge of what medical care can and cannot be expected to accomplish. Committees were established to attain these objectives. Future conferences to follow up the program were planned.

Chairman of the conference was Dr. W. A. Sawyer, medical consultant, Eastman Kodak Company, who was also a member of the survey team. Among those who represented the A. M. A. at the conference were Dr. Walter B. Martin, Norfolk, Va., member of the Board of Trustees; Dr. Elmer Hess, Erie, Pa., Chairman of the Council on Medical Service; Dr. A. J. Lanza, New York, Chairman of the Council on Industrial Health; Dr. Donald Dukelow, Chicago, of the Bureau of Health Education; George Cooley, Chicago, of the Council on Medical Service, and Dr. Ernest B. Howard, Chicago, Assistant Secretary of the A. M. A. Local arrangements for the conference were handled by Charles Lively, executive secretary of the West Virginia State Medical Association.

MEDICAL NEWS

ALABAMA

Surgical Session in Montgomery.—The Alabama division of the International College of Surgeons, with the Alabama Academy of General Practice and the Montgomery County Medical Society, will present a one day scientific program in Montgomery, Oct. 9. All Alabama physicians are invited, and it is noted that this meeting has been approved for formal postgraduate credit for members of the Alabama Academy of General Practice. Presentations will include:

Jackson L. Bostwick, Montgomery, Cervical Pain.
William Scott, Nashville, Tenn., Surgical Aspect of Congenital Heart Disease.
George C. Poore, Cleveland, Genitourinary Disease as a Cause of Nonurologic Complaints.
Lonnie W. Grove, Atlanta, Partial Gastrectomy in Peptic Ulcer with Report of 500 Cases.
Louis P. River, Chicago, Breast Cancer Diagnosis and Treatment.
Edwin L. Williams, Nashville, Tenn., Urologic Complications and Gynecologic Surgery.
Donald Miller, Chicago, Vascular and Neurological Phenomena in Orthopedics.
A. Scott Hamilton, Monroe, La., Orthopedic Problems.
James O. Morgan, Gadsden, Problems in Diagnosis and Treatment of Hyperparathyroidism.
Harry H. Jenkins, Knoxville, Tenn., Pelvic Pain.
Harold E. Simon and Byrn Williamson, Birmingham, Cancer of the Cervix.

Congressman Albert Rains of Gadsden will speak at the banquet.

CALIFORNIA

Lecture on Hyperglobulinemia.—Pietro de Nicola, associate professor, department of internal medicine, University of Pavia, Italy, will address the Southern California section of the American Association of Clinical Chemists Oct. 7 at 8 p. m. at the Hollywood Presbyterian Hospital, on "Clinical Evaluation of the Hyperglobulinemias in Connection with Some Serum Reactions."

Department of Forensic Medicine.—The University of Southern California School of Medicine, Los Angeles, has announced the formation of a full department of forensic or legal medicine. This department is an expansion of the division of legal medicine within the department of pathology, which was organized in 1948 by Dr. Frederick D. Newbarr, chief autopsy surgeon, coroner's department, Los Angeles County, who will serve as its director and professor of forensic medicine. The faculty consists of medicolegal experts, judges, attorneys, forensic chemists, and toxicologists.

CONNECTICUT

Symposium on Industrial Injuries.—A symposium on industrial injuries will be held at St. Mary's Hospital Auditorium School of Nursing, Waterbury, Oct. 9, 1: 30 p. m., under the auspices of the Industrial Health Committee, Connecticut State Medical Society; it will be sponsored by the American Brass Company, Waterbury. Dr. David M. Bosworth, New York, will discuss differential diagnosis and treatment of industrial disabilities of the back; Dr. Anthony F. De Palma, Philadelphia, shoulder injuries; Dr. J. William Littler, New York, hand injuries; and Dr. Alfonso Della Pietra, Waterbury, knee injuries.

Dr. Samuel Harvey Retires.—Dr. Samuel C. Harvey, professor of surgery in oncology at the Yale University School of Medicine, New Haven, has retired after 33 years on the faculty. He was chairman of the Yale department of clinical medicine from 1931 to 1937 and also has been chief surgeon in the Grace-New Haven Community Hospital and Dispensary. Dr. Harvey is a past president of the Connecticut State Medical Society, the Connecticut Cancer Society, and the American Surgical Association. In World War I he served with the Army Medical Corps in France and held the rank of major. During World War II he served as consultant to the U. S. Office of Scientific Research and Development. Dr. Harvey now will be William H. Carmalt professor emeritus of surgery.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Mount Carroll Honors Three Physicians.—Residents of Mount Carroll and the surrounding area held a celebration Sept. 7 in honor of Drs. Rollin B. Rice, 85, Samuel P. Colehour, 77, and Glenn E. Mershon, 76, each of whom has practiced medicine in the region for more than 50 years. Illuminated scrolls of appreciation, signed by members of the community, were presented, and a concert march, "Doctors Dauntless," written for the occasion by Director Fred Hubbell of the Mount Carroll school and municipal bands, was played for the first time. Principal speaker was Dr. James H. Hutton, Chicago, former president of the Chicago and Illinois State medical societies.

Chicago

Ophthalmological Society Meeting.—The Chicago Ophthalmological Society will meet Oct. 6 at Chicago Illini Union, 715 S. Wood St. An instruction hour in "Radioisotopes in Ophthalmology" at 4 p. m. will precede the clinical meeting, which will be presented by the department of ophthalmology, Northwestern University Medical School.

Lectures on Cancer.—Northwestern University Medical School will present a series of weekly lectures, Oct. 8 to Dec. 10, at Thorne Hall on the Chicago campus. The lectures, which are open to the profession, will be given on Wednesday evenings from 5 to 6 p. m. as follows:

Oct. 8, Pathology of Radiation Reactions, Shields Warren, Boston.
Oct. 15, Cancer Frontiers, Cornelius P. Rhoads, New York.
Oct. 22, Activities of the National Cancer Institute, Raymond F. Kaiser, Washington, D. C.
Oct. 29, Causes of Mammary Cancer in Mice, John J. Bittner, Ph.D., Minneapolis.
Nov. 5, Viruses and the Cancer Problem, Wendell M. Stanley, Ph.D., Berkeley.
Nov. 12, Hormone-Producing Tumors of the Ovary, Emil Novak, Baltimore.
Nov. 19, Metabolism of Cancer Tissue, Van R. Potter, Ph.D., Madison.
Nov. 26, "Fibrocystic" Lesions of the Bone, Granville A. Bennett, Chicago.
Dec. 3, Bronchogenic Carcinoma, Edward D. Churchill, Boston.
Dec. 10, Nutrition in Relation to Cancer, Albert Tannenbaum, Chicago.

MICHIGAN

Increase in Scarlet Fever.—According to the Michigan Department of Health, 6,846 cases of scarlet fever were reported from Jan. 1 to Aug. 28. The increase in incidence of scarlet fever, which began in 1951, represents a considerable rise over the past few years and more than doubles the total number of cases for the same period in 1950. There has been a corresponding increase in the number of cases of rheumatic fever.

Cancer Conference.—The Cancer Control Committee, Michigan State Medical Society, announces the fourth Michigan Cancer Conference, to be held Oct. 9 at the Kellogg Center for Continuing Education, Michigan State College, East Lansing. The conference, which is being held in connection with the annual training school of the Michigan Division, American Cancer Society, is co-sponsored by the Michigan Department of Health. Among the speakers will be Drs. Reader J. Hubbell, Kalamazoo, president, Michigan State Medical Society, C. Allen Payne, Blodgett Hospital, Grand Rapids, Freddy Homburger, Tufts College Medical School, Boston, and Otto K. Engelke, health officer of Washtenaw County. The discussions will emphasize the increasingly hopeful outlook for the cancer patient. Conference meetings are open to anyone interested in the cancer control program.

NEW JERSEY

Conference on Rehabilitation.—The Kessler Institute for Rehabilitation, West Orange, will sponsor an all day conference Oct. 10. Dr. Ludwig Guttmann, director, Spinal Injuries Centre at Stoke Mandeville, England, will deliver the first Fred H. Albee annual lecture on rehabilitation, in the morning. After luncheon, the following panels will be held: neurology (Donald Munro, Boston, chairman), plastic surgery (Herbert Conway, New York, chairman), urology (Herbert Talbot, Framingham, Mass., chairman), and rehabilitation and physical medicine (Howard A. Rusk, New York, chairman). Physicians desiring to attend should communicate with the Kessler Institute for Rehabilitation, Pleasant Valley Way, West Orange.

NEW YORK

Society News.—At a meeting Oct. 7, 8: 30 p. m., at the White Plains Hospital, the White Plains Clinical Society will have as speaker Dr. H. Dalton Jenkins, Harvard Medical School, Boston, who will discuss "The Present Concept of Adrenocortical Function."

Hutchings Memorial Lecture.—The annual Richard H. Hutchings memorial lecture will be delivered at 8: 30 p. m., Oct. 6, at the Syracuse University College of Medicine by Dr. M. Ralph Kaufman, Mount Sinai Hospital, who will discuss "The Psychiatrist in a General Hospital Setting."

Circulatory Disease Meeting.—The New York Society for Circulatory Diseases will meet at 8: 30 p. m., Oct. 14, at the New York Academy of Medicine. Guest speakers in a symposium on evaluation of graphic registrations in cardiology will include:

Bruno Z. Kisch, New York, Historic Introduction.
Hubert Mann, New York, Vectorcardiography.
John S. Graettinger, Pensacola, Fla., Comparison of Electrocardiographic and Vectorcardiographic Approach to the Study of Cardiac Electrical Field in the Frontal Plane.
Arthur A. Briskier, New York, New Approach to Recording of Heart Acoustics.

The meeting is open to all members of the medical profession.

New York City

Society News. — The Onondaga County Medical Society and Syracuse Academy of Medicine, meeting at 8: 30 p. m., Oct. 7, at the University Club, will hear an address by Dr. Paul Klemperer, director, pathology department, Mount Sinai Hospital, on "The Collagen Diseases."

Dr. Kallmann to Give Salmon Lectures.—The Salmon Committee on Psychiatry and Mental Hygiene announces that Dr. Franz Josef Kallmann will deliver the Thomas William Salmon lectures at the New York Academy of Medicine; Nov. 3, 10, and 18 at 8:30 p. m. His subject will be "Heredity in Health and Mental Disorder." Dr. Kallmann, who is assistant clinical professor of psychiatry at Columbia University, was one of the founders and first president of the American Society of Human Genetics.

NORTH CAROLINA

Health Association Meeting.—The North Carolina Public Health Association will meet at the Battery Park Hotel in Asheville, Oct. 9-11. On Thursday at 9 a. m. there will be a panel discussion on "Advancing Age, a New Frontier," and at 10 a. m. a symposium on "The Health of the Child." The health education section will consider the question "Is It True What They Say About Community Health?"

OHIO

Second District Meeting in Springfield.—The Second Councilor District will hold its annual fall postgraduate program at the Springfield Country Club, Springfield, Oct. 8, at 1: 30 p. m. Dr. Martin J. Cook, Springfield, will discuss ophthalmology in general practice, Dr. Robert E. Pumphrey, Dayton, office proctology, and Dr. Vergil K. Stoelting, Indiana University School of Medicine, Indianapolis, anemia. Following dinner, there will be an address by Frank G. Dickinson, Ph.D., Director, Bureau of Medical Economic Research, American Medical Association.

Northwestern Medical Meeting.—The Northwestern Ohio Medical Association will hold its annual fall program in the new Findlay Country Club, Findlay, Oct. 8, under the presidency of Dr. Charles H. Evans Jr. of Findlay. The program is as follows:

Headaches—General Considerations, Bayard T. Horton, Rochester, Minn.
Current Uses of Radioisotopes in Medicine, Gould A. Andrews, Oak Ridge, Tenn.
Thyroid Diseases in General Practice, David I. Rutledge, Boston.
Cardiac Problems in General Practice, Wright R. Adams, Chicago.

Following a luncheon, U. S. Senator John W. Bricker will address the group on "Medicine and the State."

OREGON

State Medical Meeting at Portland.—The Oregon State Medical Society will hold its annual session in conjunction with the Sommer memorial lectures, Oct. 8-11, in the Masonic Temple, Portland, under the presidency of Dr. Blair Holcomb, Portland. Three guest speakers will each deliver three of the Sommer memorial lectures. Dr. Rutherford T. Johnstone, Los Angeles, will speak on "This Age of Tension: Environment and Human Action," "The Effect of Metals and Dusts Upon Health," and "The Effects of Solvents and Insecticides Upon Health." Dr. William F. Rienhoff Jr., Baltimore, will discuss "Hyperparathyroidism: Clinical and Pathological Manifestations, Together with Treatment," "Surgical Treatment of Lesions of the Stomach and Duodenum," and "Surgical Treatment of Lesions of the Biliary Tract." Dr. R. Kennedy Gilchrist, Chicago, will present "Surgical Treatment of Ulcerative Colitis," "Principles in the Surgical Treatment of Cancer of the Colon," and "Surgical Treatment of Diverticulitis and Polypoid Lesions of the Colon."

Afternoon panel discussions will be held Wednesday on management of the elderly surgical patient, Thursday on the behavior and management of urinary tract neoplasms, and Friday on injuries to the pelvis and their complications.

Thursday at 11: 30 a. m. there will be a luncheon meeting of the Cooperating Physicians of the Oregon Physicians' Service at the Shrine Club and at 6 p. m. the dinner meeting and annual business session of the Oregon Academy of General Practice at the Mallory Hotel. The annual banquet will be held Friday at 7 p. m. in the Grand Ballroom of the Hotel Multnomah. Mr. Allan B. Kline, Vinton, Ia., president, American Farm Bureau Federation, will speak on "A Farm Leader Looks at Medicine."

The annual Oregon Medical Golf Tournament will start at 7:30 a. m. Saturday at the Portland Golf Club. At 1:30 p. m. Saturday the University of Oregon football team meets the University of California.

PENNSYLVANIA

Graduate Education Institute.—The Graduate Education Institute for 1952-1953 will open at the Williamsport Hospital, Oct. 8. Morning and afternoon sessions will be held for five days in the fall and five days in the spring. The fall program (Oct. 8, 15, 22, and 29 and Nov. 5) includes dermatology for the morning sessions and gastroenterology for the afternoon. A feature of the Oct. 22 session will be a panel discussion on the latest developments in cardiology telephoned from the Massachusetts General Hospital in Boston (J. A. M. A. **149:** 1581 [Aug. 23] 1952). The spring program (April 8, 15, and 22 and May 6 and 13) will have clinical pharmacology and pathological physiology in the morning and office diagnostic and therapeutic procedures in the afternoon.

Philadelphia

Medical History Lectures.—The section on medical history of the College of Physicians of Philadelphia will give six weekly lectures on medical history to the students of all the medical schools of this city at the hall of the college, 19 S. 22nd St. The lectures, which are open also to graduate students and other interested physicians of Philadelphia and vicinity, will be presented by Richard H. Shryock, Ph.D., and Dr. Owsei Temkin, Institute of the History of Medicine at Johns Hopkins University, Baltimore, each successive Monday evening, 7 to 8, Oct. 20 to Nov. 24.

VIRGINIA

Health Council Meeting.—The Virginia Council on Health and Medical Care will meet at 10 a. m., Oct. 9, at the Baruch auditorium of the Medical College of Virginia, Richmond. The Appomattox nutrition study and the nutrition and dental health education pilot study, carried on in Madison, Rappahannock, and Warren counties, will be discussed. For information, write Edgar J. Fisher Jr., Director, Virginia Council on Health and Medical Care, 102 E. Franklin St., Richmond 19.

WASHINGTON

Alfred A. Strauss Lecture.—The third annual Alfred A. Strauss lecture, sponsored by the department of surgery, University of Washington, Seattle, will be delivered Oct. 24 at 8: 30 p. m., at health sciences auditorium, by Dr. Warren H. Cole, professor of surgery, College of Medicine, University of Illinois, who will speak on "The Surgical Aspects of Jaundice."

Meeting of Obstetricians.—The Washington Obstetrical Association will meet Oct. 11 at the Washington Athletic Club, Seattle, under the presidency of Dr. Clarence W. Knudson, Seattle. The morning session will include presentations on "Pain in Gynecology" by Dr. Daniel G. Morton, Los Angeles, and "Induction of Labor" by Dr. J. Robert Willson, Philadelphia. At a round-table luncheon there will be further discussion of induction of labor, cancer of the cervix in pregnancy, prevention of soft tissue, and injury during labor and delivery. During the afternoon Dr. Morton will speak on "Cesarean Section," and Dr. Willson on "Essential Hypertension and Pregnancy." At the round-table banquet and symposium, Dr. Morton D. Leigh, Vancouver, B. C., will discuss "Anesthesia in Obstetrics and Gynecology." Reservations must be accompanied by a check for registration fee of $8 for members and $10 for nonmembers. This fee, which includes the cost of luncheon, social hour, and banquet, is refundable on notification before Oct. 8.

WEST VIRGINIA

Heart Symposium in Martinsburg.—A heart symposium sponsored by the Eastern Panhandle Medical Society and the West Virginia Heart Association will be held at the Hotel Shenandoah, Martinsburg, Oct. 15. Dr. Edgar W. Davis, professor of thoracic surgery, Georgetown University School of Medicine, Washington, D. C., and Dr. Bernard J. Walsh, associate clinical professor of medicine, will discuss "Diagnosis and Surgical Treatment of Congenital and Acquired Heart Disease."

All physicians in West Virginia and in adjacent areas in Maryland and Virginia are invited. Reservations for the luncheon may be made by writing to Dr. George O. Martin, Secretary, Eastern Panhandle Medical Society, Martinsburg.

WISCONSIN

Marquette Alumni Luncheon.—The annual luncheon of the Marquette Medical Alumni Association will be held Oct. 7 at the Blatz Auditorium, Milwaukee. Dr. Edward R. Annis, Miami, Fla., will speak on "Doctors as Citizens." There will be no charge for the luncheon. All Marquette alumni are invited.

Memorial to Dr. Robert Gavin.—At ceremonies conducted by the Fond du Lac County Medical Society, the new medical library was recently dedicated at St. Agnes Hospital, to the memory of Lieut. Robert C. Gavin, medical corps, United States Naval Reserve, who was lost in the South Pacific during World War II. All members of the society participated in the program by turning over a county society fund to be invested and the proceeds used as an endowment. Each individual staff member contributed, the Sisters of St. Agnes provided space and personnel for the library, and Dr. Stephen E. Gavin, father of the late Dr. Robert Gavin, established an endowment fund.

Annual Dinner of Medical Women.—The annual dinner of the Wisconsin Medical Women Branch 10 of the American Medical Women's Association will be held at 6:30 p. m. Oct. 6 at the Mathew Keenan Health Center, 3200 N. 36th St., Milwaukee. The guest speaker will be Dr. Evangeline E. Stenhouse, Chicago, national president, A. M. W. A. Dr. H. Gladys Spear, Milwaukee, will serve as moderator for a panel on psychological problems of the adolescent. Participants will be Drs. Mona Rose, F. Edith McCann, Helen J. Zillmer, Sara G. Geiger, and Mrs. Anthony Scholter of Milwaukee, Dr. Beatrice O. Jones, Racine, Helen Dunlap, Ph.D., Shorewood, and Dr. Hertha Tarrasch, Janesville.

GENERAL

Communicable Diseases in Other Areas.—According to the U. S. Public Health Service, two deaths from yellow fever were recently reported in Costa Rica, one on Aug. 19 and the other on Aug. 25. A report from Ecuador shows that 11 cases of bubonic plague occurred in the vicinity of Loji during July. These cases were in remote and primitive country; of the 11 patients, 1 died. For the first two weeks of August, two new cases were reported.

Dermatological Prize Essay Contest.—The American Dermatological Association is again offering a prize of $300 for the best essay submitted for original work, not previously published, relative to some fundamental aspect of dermatology or syphilology. Competition is open to scientists generally.

Essays will be judged on the following considerations: (1) originality; (2) potential importance of the work; (3) experimental methods and use of controls; (4) evaluation of results; and (5) clarity of presentation.

Manuscripts typed with double spacing and ample margins, together with illustrations, charts, and tables, all of which must be in triplicate, are to be submitted not later than Jan. 1, 1953, to Dr. Louis A. Brunsting, 102-110 Second Ave., Southwest, Rochester, Minn.

Meeting of Association of Blood Banks.—The annual meeting of the American Association of Blood Banks will be held at the Hotel Schroeder, Milwaukee, Oct. 9-11, under the presidency of Dr. Julius W. Davenport Jr., New Orleans.

On Thursday at 11:20 a. m. there will be a roundtable discussion on "Medicolegal Problems in Blood Banking" and on Saturday at 11 a. m. a roundtable discussion on "The National Blood Program." The following panel discussions will be held at the luncheon tables on Thursday and Friday from noon until 2 p. m.: "The Severely Bleeding Patient," "Transfusion Reactions," "Donor Requirements," "Private Community Blood Bank Serving Outlying Areas," "Erythroblastosis Fetalis," "Problems in Cross Matching," "Plasma Extenders," "Blood Immunology Including Newer Blood Groups," and "Administrative Problems."

Noise Abatement Symposium.—A national noise abatement symposium, sponsored by the Acoustical Society of America, Acoustical Materials Association, American Industrial Hygiene Association, National Noise Abatement Council, and the Armour Research Foundation of the Illinois Institute of Technology, will be held at Technology Center, 3300 S. Federal St., Chicago, Oct. 10. "The Past, Present, and Future of Noise Control" will be discussed by Mr. Ralph F. Norris at the luncheon. In the afternoon, Dr. Howard P. House, University of Southern California, Los Angeles, will talk on "The Ear and Noise," and Walter A. Rosenblith, Ph.D., Massachusetts Institute of Technology, Cambridge, Mass., on "Effects of Noise on the Behavior of People." "Safety Standards for Industrial Noise" will be presented by Stacy R. Guild, Ph.D., Johns Hopkins University, Baltimore, and "The Measurement of Hearing Loss" by Dr. Aram Glorig, Walter Reed Army Hospital, Washington, D. C.

Annual Meeting of Medical Record Librarians.—The annual convention of the American Association of Medical Record Librarians will be held at the Shoreham Hotel, Washington, D. C., Oct. 13-17, under the presidency of Marguerite E. Hoovler, Pittsburgh. Father Donald A. McGowan, director of health and hospitals, National Catholic Welfare Conference, will deliver the Sister M. Patricia memorial lecture at 1:30 p. m. in the Main Ballroom. Other participants in the program include Drs. Leonard A. Scheele and Jack Masur, Washington, D. C., Edwin L. Crosby, Baltimore, James P. Dixon, Philadelphia, Charles U. Letourneau, Montreal, Canada, Dean W. Roberts, Baltimore, John L. Wilson, Manhattan Beach, N. Y., and E. Dwight Barnett, Martin Cherkasky, Henry B. Makover, and John T. Geiger, New York. Mrs. Adaline C. Hayden, R.R.L.,

associate editor, "Standard Nomenclature of Disease and Operations," American Medical Association, will participate in the consultation clinic on standard nomenclature, which will be held in the West Ballroom Tuesday at 7 p. m.

Papers for Psychiatric Program.—The American Psychiatric Association is arranging a program to take place at the American Association for the Advancement of Science meeting in St. Louis, Dec. 29. Scientific papers will be presented during the day and a round-table discussion on "Personality of Scientific Investigators" in the evening. Members of the American Psychiatric Association who wish to present papers are requested to send a synopsis, with the title, methods, content of the paper, and the names of two discussants, to Dr. Jacob E. Finesinger, department of psychiatry, University of Maryland School of Medicine, Baltimore 1. The program committee will consider papers dealing preferably with experimental work by psychiatrists in collaboration with one or more other disciplines and containing material not previously published. From 20 to 40 minutes will be allowed for presentation. Members are also requested to suggest participants for the round-table discussion. The deadline for abstracts is Nov. 1.

Airline Plans Residency in Aviation Medicine.—American Airlines has completed plans for establishing a residency in aviation medicine. The program accords with the desire of the Interim Board of Aviation Medicine to create opportunities for civilian physicians and flight surgeons to obtain postgraduate training. In addition to broad clinical experience, the resident will be given training in all phases of the care of flying personnel, selection and maintenance of crews, transportation of patients and ill passengers, aircraft accident management, safety and health programs, altitude indoctrination, sanitation, insurance and compensation problems, and airline medical administration. He will be based at American Airlines' headquarters at LaGuardia Field in New York but will be expected to make field trips over the company's entire route. Physicians interested in this year of residency training should write to Dr. Kenneth L. Stratton, Medical Director, American Airlines, LaGuardia Field, New York Airport Station, N. Y.

Meeting of Ophthalmologists and Otolaryngologists.—The annual meeting of the American Academy of Ophthalmology and Otolaryngology will convene at the Palmer House in Chicago Oct. 12-17, under the presidency of Dr. James Milton Robb, Detroit. The president's reception will be on Sunday at 4: 30 p. m. On Monday morning Dr. Robb will speak on "As Is Your Pathology So Is Your Practice." The guest of honor, Dr. Fletcher D. Woodward, clinical professor of otolaryngology, University of Virginia Department of Medicine, Charlottesville, a former chairman of the Section on Laryngology, Otology and Rhinology of the American Medical Association, will speak on "The Widening Aspects of Otolaryngology." The scientific program includes a panel on "The Atlases of Pathology."

Tuesday at 9: 20 a. m. Dr. David G. Cogan, Boston, will deliver the Jackson memorial lecture on "Congenital Ocular Apraxia." On Tuesday afternoon there will be a symposium on "Surgical Management of Aural Cholesteatoma," an otological seminar (motion picture), and "Emergency Treatment of Cardiac Arrest in the Operating Room" (motion picture). On Wednesday a strabismus symposium and a symposium on "The Modern Treatment of Maxillary Sinusitis" will be presented. The annual academy dinner will be addressed by Capt. Eddie Rickenbacker, president of Eastern Air Lines, on "It's Not Too Late." The Wherry memorial lecture, "Experimental Observations Bearing on Meniere's Disease," will be delivered Thursday at 2 p. m. by Dr. John R. Lindsay, Chicago. At 4: 30 p. m. a program on "Allergic Management of Some Common Ear Conditions" will be sponsored by the American Society of Ophthalmologic and Otolaryngologic Allergy.

The Society of Military Ophthalmologists will hold its annual dinner meeting Tuesday. Reservations should be made with the secretary, Col. J. H. King Jr., Walter Reed Army Hospital, Washington 12, D. C. Membership is limited to ophthalmologists on extended active duty with the Army, Navy, and Air Forces. Thirty-nine alumni groups will hold dinners on Monday at 6: 30 p. m. Tickets for alumni dinners will be on sale at the registration headquarters. Tickets for the banquet will be $10. Physicians who are not members of the academy are welcome to attend as guests and to participate in all activities. Guests, however, will be required to register, and a fee of $5 will be charged.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions in the weeks ended as indicated:

Area	Sept. 13, 1952	Sept. 6, 1952	Sept. 15, 1951
New England States			
Maine	9	10	5
New Hampshire	4	5	4
Vermont	5	..	..
Massachusetts	44	40	26
Rhode Island	8	7	1
Connecticut	35	32	18
Middle Atlantic States			
New York	189	154	132
New Jersey	55	61	51
Pennsylvania	107	130	54
East North Central States			
Ohio	264	156	80
Indiana	107	112	25
Illinois	352	302	132
Michigan	274	275	110
Wisconsin	166	198	100
West North Central States			
Minnesota	405	283	47
Iowa	276	241	21
Missouri	91	139	79
North Dakota	12	20	9
South Dakota	57	39	14
Nebraska	212	211	38
Kansas	181	162	57
South Atlantic States			
Delaware	8	12	..
Maryland	11	7	11
District of Columbia	9	19	3
Virginia	87	58	14
West Virginia	49	54	10
North Carolina	36	34	18
South Carolina	12	16	17
Georgia	23	28	29
Florida	29	30	10
East South Central States			
Kentucky	162	124	21
Tennessee	43	55	34
Alabama	19	25	29
Mississippi	28	31	26
West South Central States			
Arkansas	28	25	25
Louisiana	41	12	52
Oklahoma	61	95	34
Texas	151	195	87
Mountain States			
Montana	21	16	11
Idaho	34	11	6
Wyoming	8	3	26
Colorado	45	48	67
New Mexico	30	29	6
Arizona	13	14	11
Utah	16	4	49
Nevada	3	2	4
Pacific States			
Washington	80	102	22
Oregon	24	32	14
California	189	166	158
Territories and Possessions			
Alaska	..	..	..
Hawaii	2	3	1
Puerto Rico	2	..	..
Total	4,067	3,827	1,798

Pathologists Meeting in Chicago.—The annual meeting of the College of American Pathologists will be held at the Drake Hotel, Chicago, Oct. 13-14, under the presidency of Dr. Frederick H. Lamb of Davenport, Iowa. From 1:30 to 3 p. m. on Monday there will be a medicolegal discussion on the advantages and limitations of the coroner and medical examiner system, followed (3 to 4:30 p. m.) by a panel on "Modernizing Autopsy Permit Laws."

On Tuesday the society will hold a joint meeting with the American Society of Clinical Pathologists, of which Dr. Israel Davidsohn of Chicago is president. Dr. William S. Hoffman, Chicago, will serve as moderator for the symposium on fluid and electrolyte balance Tuesday morning. Collaborators will be Drs. Donald A. Nickerson, Salem, Mass., John H. Bland, Burlington, Vt., Harry F. Weisberg, Chicago, and Thaddeus S. Danowski, Pittsburgh. They, together with Dr. Joseph D. Boggs of Chicago, will participate in a question and answer panel following the symposium. The afternoon session (2 to 4:30 p. m.) will be devoted to presentations on fluid and electrolyte disturbances in internal medicine (Dr. Henry A. Schroeder, St.

Louis), in surgery (Dr. Walter G. Maddock, Chicago), and in pediatrics (Dr. William M. Wallace, Cleveland).

The Joint Fellowship Hour (6:30 to 7:30 p. m.) will be followed by a banquet. S. I. Hayakawa, Ph.D., Chicago, semanticist, will discuss "The Task of the Listener."

CORRECTION

Lectures on Occupational Medicine.—The Saturday morning lectures on occupational medicine, which are being given by the faculty of medicine of Columbia University (*J. A. M. A.* **149:** 1657 [Aug. 30] 1952) are held from 9 to 10 a. m.

Propylthiouracil and Methimazole Therapy.—In the article by Irwin, Van Vactor, and Norris, in THE JOURNAL, Aug. 30, 1952, page 1640, in the fourth paragraph of the summary and conclusions, the figure "60%" should have been "40%."

MEETINGS

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, Chicago, Oct. 12-17. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Executive Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Palmer House, Chicago, Oct. 20-23. Dr. E. H. Christopherson, 610 Church St., Evanston, Ill., Secretary.

AMERICAN ACADEMY OF TROPICAL MEDICINE, Galveston, Texas, Nov. 13-15. Dr. Clay G. Huff, Navy Medical Research Institute, Bethesda 14, Md., Secretary.

AMERICAN ASSOCIATION OF BLOOD BANKS, Hotel Schroeder, Milwaukee, Oct. 9-11. Miss Marjorie Saunders, 3500 Gaston Avenue, Dallas 1, Texas, Secretary.

AMERICAN ASSOCIATION OF MEDICAL CLINICS, Cosmopolitan Hotel, Denver, Nov. 30-Dec. 1. Dr. Edwin P. Jordan, Box 114, Charlottesville, Va., Executive Director.

AMERICAN ASSOCIATION OF MEDICAL RECORD LIBRARIANS, Shoreham Hotel, Washington, D. C., Oct. 13-17. Miss Doris Gleason, 510 N. Dearborn St., Chicago 10, Executive Secretary.

AMERICAN CANCER SOCIETY, Park Sheraton Hotel, New York, Oct. 21-22. Dr. Brewster S. Miller, 47 Beaver St., New York 4, Director.

AMERICAN CLINICAL AND CLIMATOLOGICAL ASSOCIATION, Elmira, N. Y., Oct. 16-18. Dr. Marshall N. Fulton, 124 Waterman St., Providence 6, R. I., Secretary.

AMERICAN DIETETIC ASSOCIATION, Minneapolis Auditorium, Minneapolis, Oct. 21-24. Miss Ruth M. Yakel, 620 North Michigan Avenue, Chicago 11, Executive Secretary.

AMERICAN FRACTURE ASSOCIATION, Hotel Sherman, Chicago, Oct. 6-9. Dr. H. W. Wellmerling, 219 N. Main St., Bloomington, Ill., Secretary.

AMERICAN PUBLIC HEALTH ASSOCIATION, Public Auditorium, Cleveland, Oct. 20-24. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS, Philadelphia, Nov. 11-14. Dr. J. Earl Remlinger Jr., Suite 1101, 188 West Randolph Street, Chicago 1, Secretary.

AMERICAN SOCIETY OF CLINICAL PATHOLOGISTS, Chicago, Oct. 13-17. Dr. Clyde G. Culbertson, 1040 W. Michigan St., Indianapolis, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS, Hotel Knickerbocker, Chicago, Nov. 9-10. Dr. O. J. Pollak, P. O. Box 228, Dover, Del., Secretary.

AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE, Galvez Hotel, Galveston, Texas, Nov. 13-15. Dr. Quentin M. Geiman, 25 Shattuck St., Boston 15, Secretary.

ASSOCIATION OF AMERICAN MEDICAL COLLEGES, The Broadmoor, Colorado Springs, Colo., Nov. 10-12. Dr. Dean F. Smiley, 185 North Wabash Ave., Chicago 1, Secretary.

ASSOCIATION OF LIFE INSURANCE MEDICAL DIRECTORS OF AMERICA, Los Angeles, Oct. 21-23. Dr. Henry B. Kirkland, P. O. Box 594, Newark 1, N. J., Secretary.

ASSOCIATION OF MILITARY SURGEONS OF THE UNITED STATES, Hotel Statler, Washington, D. C., Nov. 17-19. Dr. R. R. Sayers, Armed Forces Institute of Pathology, Washington 25, D. C., Secretary.

COLLEGE OF AMERICAN PATHOLOGISTS, Drake Hotel, Chicago, Oct. 13-17. Dr. M. G. Westmoreland, 203 N. Wabash Ave., Chicago 1, Executive Secretary.

CONGRESS OF NEUROLOGICAL SURGEONS, Palmer House, Chicago, Nov. 6-7. Dr. Bland W. Cannon, 1092 Madison Ave., Memphis, Tenn., Secretary.

GREAT FALLS MEDICAL-SURGICAL CONFERENCE, Great Falls, Mont., Oct. 24-25. Dr. William E. Sullens, Box 1066, Great Falls, Mont., Chairman.

GULF COAST CLINICAL SOCIETY, San Carlos Hotel, Pensacola, Fla., Oct. 16-17. Dr. Dale E. York, 21½ E. Wright St., Pensacola, Fla., Secretary.

INDIANA STATE MEDICAL ASSOCIATION, Murat Temple, Indianapolis, Oct. 28-30. Mr. James A. Waggener, 23 E. Ohio St., Indianapolis 4, Executive Secretary.

INTERSTATE POST GRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA, Public Auditorium, Cleveland, Nov. 10-13. Dr. Arthur G. Sullivan, 16 North Carroll St., Madison, Wis., Managing Director.

KANSAS CITY SOUTHWEST CLINICAL SOCIETY, Kansas City, Mo., Oct. 6-9. Dr. Galen M. Tice, 630 Shukert Bldg., Kansas City, Kansas, Secretary.

KENTUCKY STATE MEDICAL ASSOCIATION, Columbia Auditorium, Louisville, Oct. 7-9. Dr. Bruce Underwood, 620 S. Third St., Louisville 2, Secretary.

NATIONAL GASTROENTEROLOGICAL ASSOCIATION, Hotel Statler, New York, Oct. 20-22. Dr. A. Xerxes Rossien, 1819 Broadway, New York 23, Secretary.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY, Hotel Somerset, Boston, Oct. 29. Dr. Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Secretary.

NEW ENGLAND POSTGRADUATE ASSEMBLY, Hotel Statler, Boston, Oct. 28-30. Dr. Laurence B. Ellis, 22 Fenway, Boston, Chairman.

NORTH PACIFIC SURGICAL ASSOCIATION, Spokane, Wash., Nov. 21-22. Dr. John A. Duncan, 509 Olive Way, Seattle, Secretary.

OKLAHOMA CITY CLINICAL SOCIETY, Biltmore Hotel, Oklahoma City, Oct. 27-30. Dr. N. L. Miller, 512 Medical Arts Bldg., Oklahoma City, Director of Clinics.

OMAHA MID-WEST CLINICAL SOCIETY, Hotel Paxton, Omaha, Oct. 27-31. Dr. Payson S. Adams, 1031 Medical Arts Bldg., Omaha 2, Director of Clinics.

OREGON STATE MEDICAL SOCIETY, Portland, Oct. 8-11. Dr. Robert F. Miller, 833 S.W. 11th Ave., Portland 5, Secretary.

POSTGRADUATE ASSEMBLY IN ENDOCRINOLOGY AND METABOLISM, Roney Plaza Hotel, Miami Beach, Fla., Nov. 3-8. Dr. Henry H. Turner, 1200 N. Walker Street, Oklahoma City 3, Okla., Secretary.

SAN ANTONIO TUMOR SEMINAR, Annex 4, Brooke Army Hospital, San Antonio, Texas, Nov. 1. Dr. A. O. Severance, 205 Camden St., San Antonio 2, Texas, Secretary.

SOUTHERN ELECTROENCEPHALOGRAPHIC SOCIETY, Sorrento Hotel, Miami Beach, Fla., Nov. 10-11. Dr. Irving Pine, Columbus Receiving Hospital, Columbus, Ohio, Secretary.

SOUTHERN MEDICAL ASSOCIATION, Miami, Fla., Nov. 10-13. Mr. C. P. Loranz, 1020 Empire Bldg., Birmingham 3, Ala., Secretary.

SOUTHERN PSYCHIATRIC ASSOCIATION, White Sulphur Springs, W. Va., Nov. 2-5. Dr. N. M. Owensby, Medical Arts Bldg., Atlanta 3, Ga., Secretary.

SOUTHWESTERN MEDICAL ASSOCIATION, Albuquerque, N. M., Oct. 30-Nov. 1. Dr. W. W. Schuessler, 1415 First National Bank Bldg., El Paso, Texas, Secretary.

SOUTHWESTERN SURGICAL CONGRESS, Baker Hotel, Dallas, Texas, Oct. 20-22. Miss June Marchant, 1227 Classen St., Oklahoma City, Executive Secretary.

WISCONSIN, STATE MEDICAL SOCIETY OF, Hotel Schroeder, Milwaukee, Oct. 6-8. Mr. Charles H. Crownhart, 704 E. Gorham St., Madison, Secretary.

INTERNATIONAL

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 15-20, 1953. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-8. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTER-AMERICAN SESSION, American College of Surgeons, Paulista Medical Association Bldg., Sao Paulo, Brazil, Feb. 9-12, 1953. Dr. Moacyr Eyck Alvaro, 1151 Conselacao, Sao Paulo, Brazil, Chairman.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21, 1953. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS FOR HISTORY OF SCIENCE, Jerusalem, Israel, August 3-7, 1953. Prof. F. S. Bodenheimer, Hebrew University, Jerusalem, Israel, President.

INTERNATIONAL CONGRESS ON HYDATID DISEASE, Santiago, Chile, Nov. 21-24. Organizing Committee, P. O. Box 9183, Santiago, Chile.

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP, London, England, July 20-25, 1953. Mr. W. R. LeFanu, % London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, England, Chairman.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept. 6-12, 1953. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY, Montevideo, Uruguay, March 1-7, 1953. Dirreccion General del Servico de Sanitad Militar, 8 de Octubre y Mariano Moreno, Montevideo, Uruguay, Secretariat of the Congress.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-15, 1953. Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF RADIOLOGY, Copenhagen, Denmark, July 19-25, 1953. Professor Flemming Norgaard, 10 Oster Voldgade, Copenhagen K., Denmark, Secretary General.

INTERNATIONAL CONGRESS OF THERAPEUTICS, Madrid, Spain, Oct. 16-18. Professor Armijo, Instituto de Farmacologia, Cuidad Universitaria, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4, 1953. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyoglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30, 1953. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4, 1953. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL STUDY CONFERENCE ON CHILD WELFARE, Bombay, India, Dec. 5-12. For information write: All India Save the Children Committee, 5 Carmichael Road, Bombay, India.

PAN AMERICAN CONGRESS OF THE MEDICAL PRESS, Buenos Aires, Argentine, July 12-16, 1953. Secretaria del Congress, 763 Uriburu, Buenos Aires, Argentine.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 24-29, 1953. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF MEDICINE, Montecatini, Italy, Oct. 16-18. Secretariat: Corso Trieste, 65, Rome, Italy.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICIAL THERAPY, London, England, Sept. 7-12, 1953. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C.1, England, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 23-25. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery.

ALASKA:* *Examination.* Juneau. On application in other towns where there are board members. *Reciprocity.* On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARKANSAS:* *Regular. Examination.* Little Rock, Nov. 6-7. Sec., Dr. Joe Verser, Harrisburg. *Homeopathic.* Little Rock, Oct. 27-29. Sec., Dr. Carl S. Bungart, 105 N. 14th St., Fort Smith.

CALIFORNIA: *Written.* Sacramento, Oct. 20-23. Application must be received at least two weeks prior to date of examination. *Oral for Reciprocity Applicants.* San Francisco, Nov. 8. Applicants are requested not to arrange to come to an oral examination until they receive notice from the Credentials Committee. *Oral and Clinical for Foreign Medical School Graduates.* San Francisco, Nov. 9. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento.

COLORADO:* *Reciprocity.* Denver, Oct. 14. Exec. Sec., Mrs. B. H. Hudgens, 831 Republic Bldg., Denver.

FLORIDA:* *Examination.* Jacksonville, Nov. 23-25. Sec., Dr. Homer L. Pearson, 701 Dupont Bldg., Miami 32.

GEORGIA: *Reciprocity.* Atlanta, Oct. 14-15. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

IOWA:* *Examination.* Des Moines, Dec. 8-10. Acting Director, Dr. Walter L. Bierring, State Office Bldg., Des Moines.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, Dec. 8-10. Sec., Dr. Bruce Underwood, 620 S. 3rd St., Louisville.

MARYLAND: *Examination.* Baltimore, Dec. 9-12. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1.

MICHIGAN:* *Examination.* Lansing, Oct. 15-17. Sec., Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA:* Minneapolis, Oct. 21-23. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., Dr. R. N. Whitfield, State Board of Health, Jackson 113.

MISSOURI: *Examination.* Kansas City, Oct. 24-25. Exec. Sec., Mr. John A. Hailey, Box 4, State Capitol Bldg., Jefferson City.

MONTANA: Helena, Oct. 6-8. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA:* *Examination.* Omaha, June 1953. Director, Mr. Husted K. Watson, Room 1009 State Capitol Bldg., Lincoln 9.

NEW JERSEY: *Examination.* Trenton, Oct. 21-24. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO:* Santa Fe, Oct. 13-14. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NORTH CAROLINA: *Reciprocity.* Durham, Oct. 13. Sec., Dr. Joseph J. Combs, 419 Professional Bldg., Raleigh.

OHIO: *Examination.* Columbus, Dec. 1-3. *Reciprocity.* Columbus, Oct. 7. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON:* *Examination.* Portland, January. *Reciprocity.* Portland, Oct. 10-11. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

TENNESSEE:* *Examination.* Memphis, Oct. 1-2. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS:* *Examination.* San Antonio, Nov. 13-15. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Ft. Worth.

VIRGINIA: *Examination.* Richmond, Dec. 11-13. *Reciprocity.* Richmond, Dec. 10. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke, Va.

WEST VIRGINIA: Charleston, Oct. 13-14. Sec., Dr. N. H. Dyer, State Office Bldg 23, Charleston 5.

WISCONSIN: *Examination.* Madison, January 13-15, 1953. *Reciprocity.* Oshkosh, October 9, 1952. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

WYOMING: Cheyenne, Oct. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

VIRGIN ISLANDS: *Examination.* St. Thomas, Nov. 12-13. Sec., Dr. Earle M. Rice, St. Thomas.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARKANSAS: *Examination.* Little Rock, Oct. 1-2. Sec., Mr. Louis E. Gebauer, 1002 Donaghey Bldg., Little Rock.

CONNECTICUT: New Haven, Oct. 11. Address: State Board of Healing Arts, 110 Whitney Ave., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, Oct. 20-21. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, Oct. 25. Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Oct. 10-11. Sec., Mrs. Anne Baker, 423 W. Michigan Ave., Lansing.

MINNESOTA: *Examination.* Minneapolis, Oct. 7-8. Sec., Mr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, Oct. 7-8. Director, Bureau of Examining Boards, Mr. Husted K. Watson, 1009 State Capitol Bldg., Lincoln.

OREGON: *Examination.* Portland, Sept. 6 and Dec. 6. Sec., Dr. Charles D. Byrne, State Board of Higher Education, University of Oregon, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, Dec. 5-6. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

TEXAS: *Examination.* Austin and Galveston, Oct. 17-18. Sec., Brother Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination.* Milwaukee, Dec. 6. Sec., Mr. W. H. Barber, 621 Ransom St., Ripon.

* Basic Science Certificate required.

DEATHS

Salter, William Thomas ⊕ New Haven, Conn.; born in Boston Dec. 19, 1901; Harvard Medical School, Boston, 1925; professor of pharmacology, chairman of the department, member of the executive committee, and director of graduate studies at Yale University School of Medicine; formerly research fellow, faculty instructor and assistant professor, and concurrently tutor in biochemical science at his alma mater; member of the American Association for the History of Medicine, Association of American Physicians, American Association for Cancer Research, American Society for Clinical Investigation of which he had been vice-president, American Institute of Nutrition, American College of Chest Physicians, Biochemical Society of England, American Chemical Society, Alpha Chi Sigma, Sigma Xi, Phi Beta Kappa, and Alpha Omega Alpha; fellow of the American College of Physicians; served as research fellow in biochemistry of the Harvard University Cancer Commission from 1929 to 1939; in 1942 named a member of the U. S. Pharmacopeia Antianemia Preparations Advisory Board, on which he served with distinction; two years later, elected to the U. S. Pharmacopeia Committee on Revision and took so active a role in the important Subcommittee on Scope that he was chosen its chairman for the 1950-1960 decade; in 1949 received the first Iodine Educational Bureau, Inc., award for research in pharmaceutical chemistry of iodine; associate physician, Thorndike Memorial Laboratory at Boston City Hospital from 1939 to 1941; associate physician at the Huntington Memorial Hospital in Boston from 1929 to 1939; author of "Textbook on Pharmacology," published in the spring of 1952; died in Grace-New Haven Community Hospital July 30, aged 50, of coronary disease.

Dattner, Bernhard ⊕ New York; born in Austria July 7, 1887; Medizinische Fakultät der Universität, Vienna, Austria, 1919; also a graduate in law; specialist certified by the American Board of Psychiatry and Neurology; member of the American Neurological Association and the Association for Research in Nervous and Mental Diseases; fellow of the New York Academy of Medicine; honorary fellow of the Mexican Society of Neurology and Psychiatry; associate clinical professor of psychiatry and neurology at New York University College of Medicine and assistant clinical professor of neurology at Columbia University College of Physicians and Surgeons; consultant to the United Nations World Health Organization, New York State Department of Health, and to the U. S. Public Health Service; associated with Goldwater Memorial, Montefiore, and Bellevue hospitals; joint author of "Management of Neurosyphilis," author of "Moderne Therapie der Neurosyphilis"; died Aug. 11, aged 65, of brain tumor.

Allen, Moore Lowry ⊕ Salt Lake City; born in Mount Pleasant, Utah, April 3, 1893; University of Pennsylvania School of Medicine, Philadelphia, 1924; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology; served during World War I; during World War II a member of the medical advisory board for Utah; at one time on the faculty of his alma mater; from 1933 to 1939 on the staff of the Hospital of the Protestant Episcopal Church in Philadelphia; affiliated with Dr. W. H. Groves Latter-Day Saints Hospital in Salt Lake City and Utah State Hospital in Provo, Utah; died Aug. 2, aged 59.

Owensby, Newdigate Moreland ⊕ Atlanta, Ga.; born Nov. 22, 1882; University of Maryland School of Medicine, Baltimore, 1904; specialist certified by the American Board of Psychiatry and Neurology; member and for many years secretary-treasurer of the Southern Psychiatric Association which he founded in 1935; fellow of the American Psychiatric Association; formerly on the faculty of Johns Hopkins University School of Medicine and University of Maryland School of Medicine in Baltimore; in 1934 was appointed professor of psychiatry at the University of Georgia Medical Department in Augusta; served during World War I; owner and medical superintendent of the Brook Haven Manor Sanitarium in Stone Mountain; director of the Owensby Psychiatric Clinic; affiliated with Crawford W. Long Hospital; consulting psychiatrist at St. Joseph Infirmary and Georgia Baptist Hospital; died in Piedmont Hospital Aug. 10, aged 69, of coronary thrombosis.

Ochsenhirt, Norman Charles ⊕ Pittsburgh; born in Pittsburgh Feb. 12, 1892; University of Pittsburgh School of Medicine, 1917; assistant professor of oral surgery, University of Pittsburgh School of Dentistry; formerly fellow in surgery at Mayo Foundation in Rochester, Minn.; member of the International College of Surgeons, Pittsburgh Surgical Society, the Alumni Association of the Mayo Foundation, Phi Rho Sigma, and Phi Delta Kappa; fellow of the American College of Surgeons; past president and formerly secretary of the Allegheny County Medical Society; served during World War I; affiliated with Suburban General Hospital in Bellevue, Presbyterian and Montefiore hospitals; died July 24, aged 60, of coronary occlusion.

Karshner, Rolla George ⊕ Los Angeles; University of Michigan Medical School, Ann Arbor, 1917; clinical professor of pediatrics (radiology) at University of Southern California School of Medicine; member of the American Trudeau Society, American Roentgen Ray Society, Radiological Society of North America and the American College of Radiology; specialist certified by the American Board of Radiology; affiliated with Children's Hospital, Eye and Ear Hospital, and Barlow Sanatorium; died July 12, aged 64, of carcinoma of the left lung and liver.

Cochran, Francis Bruce, Plankinton, S. D.; Washington University School of Medicine, St. Louis, 1903; died in Mitchell June 9, aged 71, of reticuloendothelial sarcoma.

Coogler, Adrian Colonna ⊕ Brooksville, Fla.; Medical College of Virginia, Richmond, 1907; died June 18, aged 65, of brain tumor.

Davis, Andrew Stubbs ⊕ San Leandro, Calif.; Medical College of Virginia, Richmond, 1926; served during World War II; died April 1, aged 51, of carcinoma of the throat.

Durham, Ray Samuel, Oakland, Calif.; University of Oregon Medical School, Portland, 1950; resident, Children's Hospital of the East Bay; died June 1, aged 31, of mesothelioma.

Fago, Paul George ⊕ Warren, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1938; died in Warren General Hospital May 25, aged 40, of carcinoma of the lung.

Fochtman, Lloyd Henry ⊕ Cozad, Neb.; John A. Creighton Medical College, Omaha, 1914; died April 5, aged 61, of coronary heart disease.

Franklin, David ⊕ Baltimore; University of Maryland School of Medicine, Baltimore, 1908; died in South Baltimore General Hospital May 1, aged 64, of cerebral hemorrhage.

Frederick, Donald Barton ⊕ Marshallville, Ga.; University of Virginia Department of Medicine, Charlottesville, 1900; vice-president of the Citizens Bank; died in Montezuma June 14, aged 73.

Fuerth, Karl, New York; Medizinische Fakultät der Universität, Vienna, Austria, 1912; died in Roosevelt Hospital, Metuchen, N. J., June 11, aged 64, of pulmonary tuberculosis.

Gelnett, William Harold ⊕ Millerstown, Pa.; Temple University School of Medicine, Philadelphia, 1935; died June 18, aged 44, of coronary occlusion.

Gillette, Harry Edwin ⊕ Pardeeville, Wis.; Milwaukee Medical College, 1908; died April 22, aged 73, of coronary thrombosis.

Grossman, Herman Paul ⊕ Providence, R. I.; Boston University School of Medicine, 1927; specialist certified by the American Board of Ophthalmology; member of the American Academy of

⊕ Indicates Member of the American Medical Association.

Ophthalmology and Otolaryngology and the New England Ophthalmological Society; served on the faculty of Harvard University Medical School, Boston; affiliated with Rhode Island, Charles V. Chapin, and Miriam hospitals; died June 5, aged 52, of uremia.

Grunfeld, Lewis, Brooklyn; Medizinishce Fakultät der Universität, Vienna, Austria, 1929; died May 29, aged 49, of hypertension.

Hamilton, Harriett Spera ⊕ Council Bluffs, Iowa; John A. Creighton Medical College, Omaha, 1912; affiliated with Mercy Hospital, where he died May 29, aged 82, of cardiac decompensation.

Hann-Kende, Fanny von ⊕ New York City; Magyar Királyi Pázmány Petrus Tudomanyegyetem Orvosi Fakultasa, Budapest, Hungary, 1914; member of the American Psychoanalytic Association and the American Psychosomatic Society; died in Harkness Pavilion, Presbyterian Hospital April 14, aged 61, of carcinoma.

Haskell, Nelson Cary ⊕ Amherst, Mass.; Medical School of Maine, Portland, 1890; member and past president of the New England Pediatric Society; served on the staffs of the Cooley Dickinson Hospital in Northampton and the Springfield (Mass.) Hospital; died in Tamworth, N. H., July 5, aged 85, of coronary occlusion.

Hedges, Leland Gilleland ⊕ Oak Park, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1921; member of the staff of the West Suburban Hospital, where he died July 31, aged 57, of cerebral embolism.

Heery, Frank Patrick, New Haven, Conn.; Yale University School of Medicine, New Haven, 1898; for many years surgeon for the police department; died June 29, aged 80.

Hirst, Elizabeth, Melrose, Mass.; Boston University School of Medicine, 1913; for many years school physician in Melrose; died June 9, aged 61, of cancer.

Horn, Samuel Wilson ⊕ Bessemer, Ala.; Emory University School of Medicine, 1916; died July 1, aged 58, of a heart attack.

Horton, Wade Hampton, Jackson, Miss.; Memphis (Tenn.) Hospital Medical College, 1899; died in Baptist Hospital July 9, aged 75, of myocardial infarction and coronary arteriosclerosis.

Hoyt, John E. ⊕ Spokane, Wash.; Northwestern University Medical School, Chicago, 1905; an Associate Fellow of the American Medical Association; served overseas during World War I; at one time practiced in Kendrick, Idaho, where he was on the school board; member of the Deaconess Hospital; drowned in Liberty Lake June 11, aged 75, when an outboard motor boat in which he was riding capsized.

Hume, Harold Clay, Savannah, Mo.; University of Kansas School of Medicine, Kansas City, Kan., 1925; died July 10, aged 55, of coronary occlusion.

Hundley, James Burnett ⊕ Danville, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; formerly health officer of Danville; died June 28, aged 72.

Irvin, George Hoff, Orrville, Ohio; Cleveland Homeopathic Medical College, 1902; served during World War I; on the local board of education; died May 28, aged 78, of biliary cirrhosis.

Israel, Isaac Joseph ⊕ Pittsburgh; University of Pittsburgh School of Medicine, 1907; served during World War I; for many years associated with the Veterans Administration; died in the Veterans Administration Hospital, Aspinwall, June 29, aged 66, of hypertensive heart disease.

Jones, Earnest Eugene ⊕ Olympia, Wash.; University of Illinois College of Medicine, Chicago, 1929; affiliated with St. Peter's Hospital; chairman of the board of directors of the Olympia State Bank; died June 28, aged 62, of coronary heart disease.

Keefe, Edward M., Cincinnati; Medical College of Ohio, Cincinnati, 1897; for many years on the staffs of St. Mary's and Good Samaritan hospitals, and surgeon for the Big Four Railroad; died July 21, aged 83, of cerebral arteriosclerosis and pernicious anemia.

Kirkendall, Edward Taylor ⊕ Columbus, Ohio; Ohio State University College of Medicine, Columbus, 1926; past president of the Columbus Academy of Medicine; assistant professor of radiology at his alma mater; served during World Wars I and II; on the staff of the White Cross Hospital; accidentally drowned in the swimming pool of his home July 19, aged 60.

Kissell, Francis Marion ⊕ Pitsburg, Ohio; Ohio State University College of Medicine, Columbus, 1916; member of the American Society of Anesthesiologists; on the staff of the Wayne Hospital, Greenville, where he died July 3, aged 61, of cerebral hemorrhage.

Lawson, Frank W. ⊕ Orange, Texas; University of Texas School of Medicine, Galveston, 1899; examining surgeon for Southern Pacific Lines; local surgeon for Gulf Coast Lines; died in Orange City Hospital July 17, aged 76, of a heart attack.

Lewis, Arthur Cuthbert ⊕ Fall River, Mass.; College of Physicians and Surgeons, Baltimore, 1893; affiliated with Fall River General Hospital; died July 6, aged 78.

Lindemann, Adolf D., New York; Independent Medical College, Chicago, 1899; Baltimore University School of Medicine, 1905; also a graduate in pharmacy; died July 13, aged 82.

Lomas, Willis Alvin, Pacific Palisades, Calif.; Rush Medical College, Chicago, 1896; for many years surgeon for the Chicago, Burlington and Quincy Railroad; died in Santa Monica June 6, aged 79, of uremia and cardiovascular renal disease.

Lorio, Lionel Francis ⊕ Baton Rouge, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1912; served overseas during World War I; affiliated with Baton Rouge General Hospital and Our Lady of the Lake Sanitarium; died June 12, aged 62, of coronary thrombosis.

Lutyens, Henry Edward ⊕ Pacific Palisades, Calif.; Chicago College of Medicine and Surgery, 1905; an Associate Fellow of the American Medical Association; member of the Illinois State Medical Society; for many years practiced in Springfield, Ill., and was at one time vice-president of the Sangamon County Medical Society; died in Good Samaritan Hospital, Los Angeles, June 21, aged 76, of congestive heart failure and aortic stenosis.

Lynch, Paul Vernon ⊕ Evansville, Ind.; Indiana University School of Medicine, Indianapolis, 1917; served during World War I; on the honorary staff, Deaconess Hospital; affiliated with Evansville State Hospital; died July 9, aged 61, of coronary thrombosis.

McGuire, William Charles ⊕ New Haven, Conn.; Yale University School of Medicine, New Haven, 1909; clinical professor of pediatrics at his alma mater; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; past president of the New Haven Medical Association; member of the board of health; served during World War I; attending pediatrician at St. Raphael's and New Haven hospitals; consulting pediatrician at Grace Hospital; died June 15, aged 65, of carcinoma of the rectum.

Mackay, Edward Hart ⊕ Clinton, Mass.; Harvard Medical School, Boston, 1898; fellow of the American College of Surgeons; school physician; on the staff of Clinton Hospital; died July 10, aged 78, of carcinoma of the sigmoid colon.

McKee, Otto Sexsmith ⊕ Clearwater Beach, Fla.; University of Buffalo School of Medicine, 1908; also a graduate in pharmacy; member of the Medical Society of the State of New York; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; served during World War I; formerly practiced in Buffalo, where he was consulting surgeon in otolaryngology in Buffalo General, Children's, and Millard Fillmore hospitals; died July 19, aged 69, of pulmonary infarction and femoral phlebitis.

Malcolm, William Alexander ⊕ Peoria, Ill.; University of Illinois College of Medicine, Chicago, 1919; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; served during World

Wars I and II; on the staff of St. Francis Hospital, where he died July 18, aged 57, of acute coronary occlusion and arteriosclerosis.

Martin, James Cordie ✠ Cullman, Ala.; Chattanooga (Tenn.) Medical College, 1905; died June 1, aged 73, of injuries received in an automobile accident.

Merrill, Walter Hibbard ✠ Washington, D. C.; Columbian University Medical Department, Washington, D. C., 1901; at one time on the faculty of his alma mater; formerly roentgenologist for the District of Columbia Health Department; specialist certified by the American Board of Radiology; served on the staffs of the Tuberculosis Sanatorium in Glenn Dale, Md., and the Garfield Memorial Hospital; died July 23, aged 79, of cerebral hemorrhage.

Miller, Loren Bertrand, Wichita, Kan.; Dunham Medical College, Chicago, 1901; for many years on the staff of the Wichita Hospital; died July 17, aged 81, of carcinoma.

Miller, Thurlow Spragge, San Francisco; Detroit College of Medicine, 1892; died July 3, aged 80, of hypertensive and arteriosclerotic heart disease.

Mills, Herbert Raphael ✠ Tampa, Fla.; Rush Medical College, Chicago, 1910; specialist certified by the American Board of Pathology; founding fellow of the College of American Pathologists and fellow of the American Society of Clinical Pathologists; at one time director of the local laboratory of the Florida State Board of Health; served during World War I; affiliated with St. Joseph's Hospital, where he died June 27, aged 69, of acute monocytic leukemia.

Moore, Garfield B. ✠ Chicago; Meharry Medical College, Nashville, Tenn., 1917; died in Provident Hospital July 9, aged 65, of cerebral thrombosis, hypertension, and coronary sclerosis.

Moulden, William Raymond ✠ Washington, D. C.; Columbian University Medical Department, Washington, 1900; for many years on the staffs of the Central Dispensary and Emergency Hospital and Georgetown Hospital; died July 4, aged 75, of carcinoma of the urinary bladder.

Murt, Roland Sumner, Philadelphia; Temple University School of Medicine, Philadelphia, 1933; member of the Industrial Medical Association; served during World War II; died July 12, aged 44, of lobar pneumonia.

Musser, Fred Cowley ✠ Los Angeles; Detroit College of Medicine and Surgery, 1915; on the staff of the Hollywood Presbyterian Hospital; died July 1, aged 64, of hypertensive arteriosclerotic heart disease.

Naylor, Archibald Enos ✠ Detroit; University of Toronto Faculty of Medicine, Toronto, Canada, 1909; Detroit College of Medicine, 1912; on the staff of Harper Hospital; died in Mitchell Bay, Canada, June 28, aged 65, of coronary thrombosis.

Nesbit, Alice Pitkin, Chicago; Northwestern University Woman's Medical School, Chicago, 1900; served on the staff of the Evanston (Ill.) Hospital; died in Bethany Methodist Hospital July 21, aged 76, of coronary thrombosis.

O'Hern, Maurice C. ✠ Chicago; Bennett Medical College, Chicago, 1914; assistant clinical professor of pediatrics at Stritch School of Medicine of Loyola University; specialist certified by the American Board of Pediatrics; affiliated with Little Company of Mary Hospital in Evergreen Park, and Mercy Hospital; served during World War I; died July 24, aged 74, of chronic myocarditis and nephritis.

Ohlbaum, Clarence Joseph ✠ Brooklyn; Eclectic Medical College, Cincinnati, 1921; on the staff of the Prospect Heights Hospital; died July 11, aged 55, of coronary thrombosis.

Osborn, Horatius Dwight, Excelsior Springs, Mo.; St. Louis College of Physicians and Surgeons, 1922; died April 14, aged 51.

Payne, John Bosworth, Arlington, Va.; College of Physicians and Surgeons, Baltimore, 1896; died in St. Elizabeth's Hospital, Washington, D. C., July 1, aged 79, of arteriosclerosis and pulmonary embolism.

Powell, Everett Newman, Corydon, Ky.; University of Louisville School of Medicine, 1903; formerly county health officer; member of the staff of Methodist Hospital; died June 26, aged 76, of myocarditis.

Quinn, Thomas D'Arcy McGee ✠ San Francisco; University of California Medical School, San Francisco, 1902; for many years city physician; on the staff of St. Luke's Hospital; died June 4, aged 77, of coronary disease.

Reeves, George William ✠ Farmington, Mo.; Beaumont Hospital Medical College, St. Louis, 1898; died June 21, aged 80, of injuries received in an automobile accident.

Ringrose, Frank M. ✠ Boonville, N. Y.; Syracuse University College of Medicine, 1894; died in Faxton Hospital, Utica, June 18, aged 85, of coronary thrombosis.

Sanders, Henry Clay Jr. ✠ Claremont, N. H.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; formerly vice-president of the New Hampshire Medical Society; died June 7, aged 80, of bronchopneumonia and coronary artery disease.

Sankey, Brant E., New Castle, Pa.; Cleveland Medical College, Homeopathic, 1895; died June 9, aged 79.

Siebner, Frederick ✠ Norfolk, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1926; health officer of the town of Norfolk; on the staff of Potsdam (N. Y.) Hospital; died June 8, aged 51, of coronary thrombosis.

Snyder, Oscar Burton ✠ Greensburg, Pa.; University of Pittsburgh School of Medicine, 1909; fellow of the American College of Surgeons; on the staff of Westmoreland Hospital, where he died June 6, aged 72, of cerebral hemorrhage.

Van Duyne, Sarah Elizabeth, Montclair, N. J.; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1899; died in the Community Hospital June 28, aged 79, of carcinoma.

DIED WHILE IN MILITARY SERVICE

Tracy, Jay Benjamin Jr., St. Albans, N. Y.; born in Baltimore Dec. 24, 1921; University of Pennsylvania School of Medicine, Philadelphia, 1947; in 1942 entered the Naval Reserve and on May 5, 1943, accepted a commission as an ensign, H-V(P)USNR; resigned this commission shortly thereafter and re-enlisted in the Navy's V-12 program; served a one year rotating internship at the Graduate Hospital of the University of Pennsylvania and was a resident in otolaryngology and bronchoesophagology at that hospital; commissioned a lieutenant (jg) in the medical corps, USNR on Nov. 16, 1950, and called to active duty in July, 1951; he served at the Naval Hospital, Philadelphia, and at the Naval Hospital at St. Albans, where he was serving at the time of his death, June 9, aged 30, of injuries received when struck by an automobile.

Pender, Bernard Hyson ✠ Lieutenant, United States Navy, Waukegan, Ill.; born in Mechanicville, N. Y. Oct. 17, 1921; University of Rochester School of Medicine and Dentistry, Rochester, N. Y., 1945; formerly resident in anesthesia at the Huron Road Hospital in Cleveland; entered the U. S. Naval Reserve in June 1945 as a lieutenant (jg); later transferred to regular navy; received World War II Victory Medal; served at Pusan and Inchon and elsewhere in the Korean area while aboard the hospital vessel, USS Haven; died Jan. 18, aged 30, while attached to the U. S. Naval Hospital, Great Lakes, Ill.

Ruth, Weldon Kenneth ✠ Colonel, M.C. United States Army, Denver; University of Oklahoma School of Medicine, Oklahoma City, 1933; entered the medical corps of the U. S. Army as a first lieutenant in December, 1936; rose through the various ranks to that of colonel; served as resident at Fitzsimons Army Hospital, where he died May 2, aged 43, of myocardial insufficiency.

FOREIGN LETTERS

ITALY

Italian Society of Endocrinology.—The Italian Society of Endocrinology met in Pisa under the chairmanship of Professor Pende, from the University of Rome, Professor Cassano, from the University of Pisa, and Professor Antonietti, from the University of Genoa. Numerous clinicians and endocrinologists from northern and central Italy were present.

Professors N. Pende and V. Pende, from the University of Rome Institute of Medical Pathology, reported on five patients who had infantile myxedema with generalized muscle hypertrophy and strength comparable to that of a strong adult. After therapy with thyroid and anterior hypophysis extracts, the mental and physical development improved and the myxedematous facies became normal, but muscle hypertrophy and hyperergy persisted. Two patients had hypercreatinemia, which is not usually seen in states of hypothyreosis. The speakers advanced the hypothesis that the excess muscle anabolism may cause, in congenital and adult hypothyreosis, muscle hypertrophy with hypertonia and increased contractile energy. The excessive development of muscles in patients with myxedema suggests also a possible associated dysfunction of the parathyroid glands and the adrenal cortex. The parathyroid glands may participate in the metabolism of creatine and especially in its phase of phosphorylation and synthesis into phosphocreatine. The role of the adrenal cortex in muscle tissue changes is already known. The speakers concluded that their cases may be classified among the forms of myxedema of a pluriglandular type.

Professor Gaspersic, from the University of Siena Medical Clinic, reported on relationships between diabetes and internal secretion. From her serologic analysis of 18 patients with diabetes of various stages and on the basis of the data inferred from the anamnesis and the examination, the speaker believes that when Hanger's and Maclagan's tests are strongly positive they may give useful indications as to which endocrine gland is causing dysfunction of the carbohydrate metabolism. When a somatic picture or a disease of a definite gland is associated with the serologic data the diagnosis is certain.

Drs. Fieschi and Lamperi, from the University of Siena Institute of Medical Pathology, reported their results of cortisone and renal extract therapy in patients with chronic nephritis in the second stage with a picture of severe nephrosis. Improvement of the tubular function followed cortisone therapy; increased glomerular filtration and a greater quantity of blood circulating in the kidneys were seen after administration of renal extracts. These effects occurred simultaneously when the two drugs were combined. The speakers discussed the mechanism of action of this treatment and attributed to cortisone the effect on tubular cells and to renal extracts mainly a "vasculotropic" action.

Drs. Tronchetti and Nello, from the University of Pisa, reported that when therapeutic doses of sodium salicylate were given to normal persons only the 11-oxycorticosteroids increased and not the 17-ketosteroids. They injected rabbits intravenously with a dose of sodium salicylate equal to the average dose given to human beings. They observed an increase in the thickness of the adrenal cortex, especially in the zona fasciculata, with cellular hypertrophy, diminution of ascorbic acid, and lipids depletion. The other endocrine glands underwent changes in part analogous to those produced by cortisone, especially regressive alterations of the thymus and the semen line of the testes, thyroid hyperactivity, and increased glycogen in the liver. These findings seem to suggest a stimulating action of sodium salicylate on the adrenal cortex, perhaps through the hypophysis. According to the speakers, not all the antirheumatic and antiphlogistic action of sodium salicylate rests in its adrenal cortex stimulating activity. They believe that part of the therapeutic action of salicylate preparations is attributable to a cortisone-like effect.

Dr. Ferrari, from the University of Padua, studied, by means of radiology, the dysfunction of the digestive system and the extrahepatic biliary ducts in patients with Basedow's disease at various stages. He observed acute and severe gastroenteric manifestations, such as enteric type of disturbances and clinical pictures simulating duodenal ulcer. More frequently he observed mild gastroenteric manifestations with chronic tendency, such as disorders to tonus and of the movements of the biliary ducts and disorders of secretion. According to the speaker, these disturbances may have some connection with hyperthyroidism, as is shown by the patient's sensitivity to antithyroid therapy.

LONDON

Chloramphenicol.—The first cases of death in this country attributed to chloramphenicol (chloromycetin®) have now been recorded. Three such cases are reported in a recent issue of the *British Medical Journal* (**2**:423-427 [Aug. 23] 1952). All three were children (aged 4, 7½, and 6 years) who received chloramphenicol for the treatment of pertussis. In each case treatment was maintained for long periods: (1) 20 gm. over a period of about 27 days, (2) 28 gm. in a period of 44 days, and (3) 12 gm. over a period of 24 days. In each case jaundice was the initial sign of toxicity, and the time between the termination of chloramphenicol therapy and the onset of jaundice was 12 days, 5 days, and 1 month. The outstanding features at necropsy in each case were severe anemia; extensive hemorrhages into the skin, mucous membrane, serous membranes, and the parenchyma of most organs; absence of lymphadenopathy; and a bone marrow grossly deficient in all blood elements. It is generally recognized that one of the major factors in the group of deaths is the indiscriminate use of the drug, and the general feeling is that, if, as must inevitably now occur, the drug is used with circumspection and only in cases in which it is really indicated, the risks are probably not of great import, provided the patient is carefully watched during the time the drug is being administered.

Modern Medicine.—The following excerpt from a letter from a general practitioner to *The Spectator* is reproduced without comment. *The Spectator* is renowned in this country for the objectivity of its comments on current affairs and for its high literary standards.

"Under the National Health Scheme we find ubiquitous 'health visitors,' usually in the form of smart young women who visit our patients in shiny cars without as much as 'by your leave,' and who question them about their progress, and as to whether the doctor has been to see them. The object presumably is to make sure that the doctor is not keeping them away from work too long. The doctor cannot be relied on to use his own judgment in the matter. Such a visitor recently visited one of my patients who was too lame to get out of bed. In the course of conversation she elicited the fact that I had not visited the patient to certify her incapacity for work on the day on which I had given her a certificate, although it was perfectly obvious that the patient was quite incapable of walking. The health visitor accordingly secured a signed statement from the patient to that effect. All this without my knowledge. The result was a fine of £5."

Incidence of Enteric Fever.—The latest returns show an unusually high incidence of paratyphoid fever. The figures for the week ending Aug. 2 are the highest for any week during the last nine years: 130 cases of paratyphoid fever and 5 cases of typhoid fever. The figures for paratyphoid fever for the previous week was 75, while for the week ending Aug. 9 it fell to 62. Most of the cases have occurred in Wales, where 327 cases have been seen during the last 12 weeks.

The Ministry and Defamation Proceedings.—The British Medical Association has received assurance from the Ministry of Health that, in the event of proceedings for defamation against a physician arising out of his entries on a hospital patient's

The items in these letters are contributed by regular correspondents in the various foreign countries.

case record by means of their loan to, and use by, the Ministry of Pensions or the Ministry of National Insurance, the Minister of Health will indemnify the physician against any damages that may be recovered and against all reasonable costs that he may incur in defending the proceedings, provided the minister has complete control over the conduct of the defense. This assurance also covers medical practitioners called on to disclose confidential information before tribunals.

PARIS

Electroencephalograms, Corticotropin, and Cortisone.—At the Hospital for Sick Children, Prof. R. Debré, Dr. P. Mozziconacci, and Dr. J. Nekhorocheff studied the electroencephalograms of 74 children treated with corticotropin and cortisone and observed alteration in 38 of them. In 17 of these, alterations consisted in slow waves on the encephalogram of rest; 17 others showed positive reactions to intermittent luminous stimulation. Of 34 patients with Bouillaud's syndrome, 18 had at least one abnormal electroencephalogram; and of 18 patients with reticulosis and leukosis, 12 had abnormal electroencephalograms. The possible coincidence of constitutional electrical alterations and of modifications to the diagram owing to the disease itself (anemia of nervous centers and cerebral edema) has to be taken into account to arrive at a correct estimation of the results obtained. Nevertheless, in 20 cases the altered diagrams remained attributable to the hormonal treatment; according to the authors, cortisone provoked electrical alterations more frequently than corticotropin.

The duration of treatment is an essential factor; out of 17 children subjected to treatment less than 15 days, only 3 presented electrical alterations. Moreover, Debré and his associates stressed that treatments altering the electroencephalogram are those provoking definite clinical signs of hypercorticalism: rounded aspect of the face, vergetures, pilosity, acne, and noticeable increase of weight. In such cases the diagram has been altered in one out of two cases, and when such signs were not present it was altered only in one case out of five.

Professor Debré concluded that electroencephalograms are to be constantly and carefully observed during long treatments, as the presence of slow waves, or of points of waves, is a probable indication for discontinuing the treatment. Moreover, Debré insisted on the interest of these studies for the precise determination of the posology of hormones. He presented the results of his works at a recent meeting of the Medical Society of the Paris Hospitals. In the course of the discussion, Dr. Klotz reminded that, according to experimental works, cerebral circulatory disorders occur during the administration of corticotropin, which might explain the anomalies of electroencephalograms. Cathala insisted on the presence of a characteristic neurological syndrome during corticotropin therapy; such syndromes are often foretold by disturbances of the electroencephalograms and, in his opinion, occur with predisposed environments. Hazerad reported that he performed electroencephalography in adrenal deficiency and that he noted rhythmic disorders in these patients, which were corrected with cortisone.

Implants of Thyroid Bodies in Chronic Rheumatism.—In 1943, Mandel and Gyri innovated the method of implants of human thyroid bodies, and, at the end of 1951, they published the results obtained in 50 patients thus treated. Etienne Martin and his associates (Dijon) tried this method by using pathological thyroid bodies (goiter and Basedow) or thyroid bodies of healthy calves in 19 cases of chronic rheumatism. Implants were kept at –20 F till they were used. A fragment the size of a nut was implanted between the muscle and the fascia in the region of the rectus abdominis muscle. Incidents were very few. In 15% of cases, Basedow implants brought about the small signs of hyperthyroidism: tachycardia, tremor, insomnia, and transient disorders lasting a few days only. Sometimes there was also a 20% increase of the basal metabolism. Patients experiencing these incidents were those reacting best to the treatment. In 21% of cases immediate results were observed within a few hours after the implantation: first, alleviation of the painful phenomena and then resumption of articular mobility. In 50% of cases effects were observed two to five days after the implantation and the general condition was improved. Failures were experienced in 21% of cases. With slower results (from a few days to five months) only 15% of relapses were noted, but even these relapses were sensitive to a further implantation bringing about the same improvement. Of the patients subjected to this treatment 95% suffered from severe rheumatism developing for years and resisting all therapy, even hormonal. The most spectacular results were noted in patients with spondylarthritis ankylopoietica and in those with spondylarthritis deformans. A remarkable result was achieved in a case of severely evolutive psoriatic rheumatism resistant to cortisone treatment.

Serious Accidents Owing to *p*-Aminosalicylic Acid.—Though *p*-aminosalicylic acid is now considered one of the classical weapons against tuberculosis, rather serious accidents were lately reported. J. Boudin and J. C. Job, of the Clinic of Neurology of the La Salpétrière Hospital (Professor Alajouanine's ward) reported that a fatal case occurred the day after a first and unique intravenous perfusion of *p*-aminosalicylic acid was given to a 60-year-old female patient, with spastic paraplegia and affected lungs. This fatal accident followed the administration of 1 gm. of streptomycin and the perfusion of 500 cc. of a solution containing 15 gm. of *p*-aminosalicylic acid injected in six hours. Autopsy performed two hours after the death revealed a lesion on the fifth and sixth thoracic vertebrae, which had compressed the spinal cord by angulation. There was no cerebromeningeal or coronary lesion, but there was a phlebothrombosis at the site of the injection. According to the authors, the death was due to a peracute form of pulmonary embolism. This is the first reported case of a death following an intravenous injection of *p*-aminosalicylic acid; all accidents previously described consisted only in late venous obliterations, owing to repeated perfusions.

At a meeting of the Medical Society of the Paris Hospitals, A. Tzank and E. Sidi reported one case of cutaneous sensitization to *p*-aminosalicylic acid, which occurred in a female patient working in a laboratory of pharmaceutical products, who was affected with a dermatitis of the face and hands of professional origin. Epidermal tests with *p*-aminosalicylic acid revealed a very noticeable positivity. The check by injection of a dose of 0.25 gm. of *p*-aminosalicylic acid brought about not only recurrence of the eruption but also a resumption of positive results of the cutaneous tests and the reappearance of alarming general and febrile accidents. The authors conclude that, as is the case with so many other products, it appears that even slight cutaneous sensitivity exposed the patient to serious accidents when the injection is made. Such accidents can be prevented by means of cutaneous tests previously performed. In fact, when a patient is to undergo *p*-aminosalicylic acid therapy, it is necessary to inquire whether he has previously had any dermatitis provoked by the drug. In his summary, Tzank stressed that the administration of normal doses of *p*-aminosalicylic acid to such a patient, without the knowledge of such antecedents, led to the same fatal result as in Boudin's case.

Titration of Carbon Monoxide in Air.—P. Revel and P. Duquénois have evolved a method permitting the titration of small concentrations of carbon monoxide in the air. It is of special interest when, with other methods, the extraction of carbon monoxide becomes too delicate and inaccurate. It may be of interest in industrial medicine for the analysis of the atmosphere of workshops likely to bring about chronic or subacute intoxications. Last year, the authors already presented to the Society for Forensic Medicine a photometric technique of E. Wolff's reaction for the determination of the carbon monoxide level in the blood. Acting on the same principle, they evolved a method for the analysis of the atmosphere. It consists in passing a given volume of air into a given quantity of blood, which is then subjected to aceto-acetic flocculation and photometric measure.

A 5.5 liter graduated flask (for richer industrial atmospheres a 2.5 liter flask is used) is provided with two stopcock tubes, one on the top and the other at the bottom. This flask is filled with water, which is partly poured out on the spot where the air is to be analyzed, till only 500 cc. of water remains; then 5 liters (respectively, 2.5 liters) of air is introduced into the flask. In the laboratory, the 500 cc. of water remaining in the

flask are drawn through the bottom stopcock tube and the partial vacuum thus obtained allows the introduction, through the top stopcock tube, of the following solution (prepared extemporaneously and avoiding its alteration by exposure to air): 75 gm. of powdered industrial sodium thiosulfate, 350 cc. of distilled water, and 75 cc. of sodium lye. The flask is shaken several times for 15 minutes, in order to absorb the oxygen and the carbonic gas of the air, while alkali is retaining the sulfurous acid. Water is then introduced through the inferior tube connected with a Mariotte's flask till the pressure equilibrium (one-fifth of the original air) is obtained. Then air is passed in a solution of defibrinated human blood, diluted to one-fifth. The slow and regular passage of air is effected by microdiffusion. Then estimations are arrived at. The calibration curve is built up by means of giving volumes of air, in which pure carbon monoxide has been introduced. Unless an important modification is brought to the technique, the blood of animals is unsuitable for this method. In their communication to the National Academy of Medicine, Revel and Duquénois stressed that this method is very reliable; no error was found up to the limit of sensitivity. Its specificity has been checked by means of tests with air free from carbon monoxide; they never yielded any filtrate of pink coloration. On the contrary, a pink filtrate obtained can be verified with the spectroscope in a positive check. With repeated titrations under similar conditions only differences of the order of one to two are obtained on the photometer.

SWEDEN

Systematic Treatment of Heart Disease.—Dr. Gunnar Biörck of the town of Malmö proposes that patients with certain forms of heart disease should enjoy the benefits available for tuberculosis patients in a well-organized and permanent system of stations or dispensaries staffed by specialists. In Sweden there are at least a quarter of a million persons who suffer from some disease of the cardiovascular system. They may be classed in four main groups, according to whether they suffer from arteriosclerosis (including cardiosclerosis), hypertonia, heart neurosis, or valvular disease of the heart. In this last group there may be anything from 10,000 to 30,000 persons for whom, in some instances, there is a prospect of radical improvement owing to recent advances in the surgery of the heart. In the same group after an attack of rheumatic fever there is now also a prospect of preventive treatment with penicillin, corticotropin, or cortisone. At the present time there are many mitral stenosis patients scattered over Sweden who might benefit from an operation if they could be discovered and dealt with in time. Dr. Biörck is convinced that throughout the country there are many patients who suffer from mitral stenosis amenable to operation and who are unaware of this possibility. Their physicians should decide if such cases are operable. Many such cases may have become too advanced to qualify for an operation, and only a short time ago neglect of this opportunity could hardly be criticized, seeing how new the operative treatment of heart disease is. Dr. Biörck's scheme for dealing with this problem is quite elaborate. Its central feature is a heart disease dispensary to be staffed by specialists and to collect and keep records of all the patients treated for rheumatic fever in various hospitals throughout Sweden. Hitherto these patients have been more or less left to themselves during the interval of a decade or two between the primary infection and a definite lesion of the heart. The old objection may be raised that once more some of a general practitioner's patients are to be filched from him by interfering specialists. But there should be plenty of scope for cordial cooperation between the two, with a team of heart specialists playing happily into the hands of the private practitioner.

Infants' Hospitals.—The eight infants' hospitals or homes administered by the City of Stockholm Child Welfare Board have recently been the subject of special investigations and experiments by Dr. Ingvar Alm, in the hope that economies might be effected without interfering with the efficiency of these establishments. As he points out in *Nordisk medicin* for July 4, 1952, the cost of these establishments in 1950 were 13 kroner ($3.59) per head per day, 64% of the total cost coming on the staff account. The capital value of a member of the staff (a full-time infants' nurse employed permanently) has been put at about 120,000 kroner ($32,232.00), and one member of the staff is required for every 1.9 infants. In 1950, when 416 infants were admitted to these homes, it cost 750,000 kroner ($201,450.00) to run them, and, although there were waiting lists on several occasions, only 88 to 90% of the available beds were always in use. In his survey of these establishments as a whole and after special investigations in one of them, Dr. Alm concludes that both economy and efficiency could be effected by distinguishing between, and providing for, two different types of infants' homes. The one should be designed for patients who stay in homes for long periods, and it should retain the features likely to assure a homely atmosphere. The other type should be designed for patients with acute cases, often requiring residence of only brief duration. With regard to acute cases and the prevention of hospital infections, Dr. Alm suggests that it is very exceptional for the infants' parents to be responsible for conveying the infectious diseases of childhood. He has found that in infants' homes with 25 to 30 beds, as many as six to eight hours are spent every day by the nursing staff on the preparation of food. He wondered whether it would be possible to transfer all this work to the kitchen staff and also to simplify matters by depending more on commercial brands of infants' foods. To study these possibilities closely, Dr. Alm introduced into an infants' home, for several months, a system of feeding based exclusively on commercial brands of foods. During another period of several months he realized his scheme of diverting all the preparation of food from the nursing to the kitchen staff, the nurses being required to distribute the food but not prepare it. On the whole, the outcome of these experiments was satisfactory, and Dr. Alm suggests that to encourage the kitchen staff to take over the complete preparation of food it is desirable to provide kitchens with up-to-date equipment.

Cancer of the Stomach.—The newly created Swedish National Association for Combating Cancer has stated in a manifesto to the public that the cancer mortality is rising. Prof. Gunnar Nyström of Uppsala is prepared to endorse this statement as far as the absolute number of cancer deaths is concerned. But when the distribution of the cancer deaths is studied in different age groups and according to sex, it would seem, according to official Swedish statistics, that the mortality from cancer of the stomach in middle-aged men is definitely falling. Further, during the last decade there has been practically no change in the cancer mortality of men of all ages, while the cancer mortality for women of all ages has continued to rise. Henschen has shown that in Stockholm between 1905 and 1945 the gastric cancer mortality fell rapidly, being down in 1945 to 43 per 100,000 live population. In the earlier years of this period the gastric cancer mortality was fairly constant, at the rate of 55 to 63 per 100,000. Professor Nyström has explored the possibility that this change for the better may be due to a high recovery rate for operations for cancer of the stomach. This recovery rate has, to be sure, risen greatly. Yet it can account for very little of the fall of the gastric cancer mortality, which must surely reflect a fall in the gastric cancer morbidity. Henschen's suggestion that the falling gastric cancer mortality rate is the outcome of a higher standard of living with better food must, of course, be substantiated by more research in this field, but, whatever the cause of this phenomenon, it seems to be an unquestionable fact. Another reassuring fact is that the sarcoma mortality for all ages has shown practically no rise between 1921 and 1949. It was 4.7 per 100,000 in the 5 year period 1921-1925, and it was 4.8 in the 4 year period 1946-1949. Far less cheering are the figures concerned with the cancer mortality for women of all ages and for persons over 70 of both sexes. Between 1936 and 1949 the cancer mortality for men of all ages per 100,000 was almost unchanged, from 127.7 to 128.3, whereas in the same period for women of all ages there was a rise of from 139.1 to 142.4. According to official statistics, it was found that in 1948 and in 1949, the cancer deaths after the age of 80 accounted for approximately one-seventh of all the cancer deaths in Sweden. Over the age of 70 the cancer mortality has risen from 774.6 per 100,000 in 1921 to 976.5 per 100,000 in 1949.

CORRESPONDENCE

STERILITY OF MARKET COTTON

To the Editor:—In the interests of the thousands of physicians and other professional personnel throughout the world who weekly refer to THE JOURNAL, we feel it incumbent on us to direct your attention to the article entitled "Sterility of Market Cotton," by J. H. Silliker and E. P. Hess (*J. A. M. A.* **149:**1374-1376 [Aug. 9] 1952). This article is a matter of concern to us since it not only fails to utilize established statistical and technical bacteriologic concepts of sterility testing but, by frequently specious reasoning, arrives at a wholly misleading conclusion with respect to the sterility of various brands of absorbent cotton currently available on the open market.

Although the term sterility is, of course, absolute, its use in the strict sense necessarily falls within the limitations of the methods currently available to detect contamination. It is general knowledge that, for most of the many thousands of pharmaceutical and surgical items bearing the designation sterile, it would be impossible statistically to detect all contaminated samples without wholly "destructive" sampling or, at the very least, consuming an unreasonable portion of each manufacturing batch.

In the case of sterile market cotton, sterility is accomplished by highly specialized methods designed to give an extremely high degree of assurance from a statistical viewpoint; sterility tests, in essence, merely serve as running checks on the procedure. Control of the sterilizing process, in this company at least, is assured not merely by elaborate recording temperature controls but by exhaustive and repeated studies of the conditions existing in all parts of the autoclave during the processing of standard loads to determine with absolute certainty that sufficient amounts of heat and steam to afford a very large margin of safety have reached all parts of the sterilizer load and that a sufficient time factor has been allowed well in excess of theoretical requirements. In addition, strategically placed samples of the product inoculated with known heat-resistant spore-forming organisms routinely are included. These, in addition to other suitable samples, are tested bacteriologically for sterility on a statistical basis. This responsibility for adequate sterility testing and the maintenance of a sterile product, aside from being obligatory under the law, is keenly felt by all reputable manufacturers and has resulted in intensive programs of sterility testing studies. As a result, the control laboratories of the industry have acquired a comprehensive knowledge of the shortcomings and limitations of such tests, as well as a broad understanding of the interpretation of the data accumulated. Evaluations of this nature are based on continuous study of the precise conditions existing in the aseptic room and of the various aseptically conducted manipulations therein by specially trained technicians. Any data collected without adequate regard to such factors are therefore subject to question.

The authors of the paper to which exception is being taken appear to have either overlooked or omitted several pertinent details. Although one is led to believe that U. S. Pharmacopeia recommendations were their guide, striking exceptions to the U. S. P. specifications with respect to the culturing of solids were employed. The procedure, as presented, appears cumbersome and places unduly optimistic dependence on the use of benzalkonium chloride as a sterilizing agent. Benzalkonium chloride in our hands has been regarded as no more than a bacteriostatic agent, and we have no assurance, for instance, that wetting down the package with such a solution in the manner described by the authors may not actually serve to introduce organisms into an otherwise sterile field. Furthermore, manipulative or chance contamination is, in fact, discounted, since statistically the controls utilized in the study are inadequate with respect both to number and to potential time of manipulative exposures.

In the Silliker and Hess report, it is stated that 14 positive culture tubes in 413 tests (i. e., one in 29.5), representing 85 rolls of cotton, were encountered. This observation apparently is interpreted as indicating that 14 of the 85 rolls of cotton were unsterile and not only is offered as evidence of laxity on the part of the Food and Drug Administration and the manufacturers concerned but has prompted the authors to considerable theorizing in an effort to explain the survival of the autoclaving process by the allegedly contaminating organisms. Conclusions of this type are, of course, both dangerous and unwise unless adequately substantiated by unequivocal data indicating that the cotton itself was the source of the organisms found. Without adequate knowledge of the aseptic area in which the tests were performed, past history of manipulative proficiency of the operators performing the tests, and controlled checks on the technique itself, it is statistically far more likely that the organisms were introduced into the culture tubes from a source other than the cotton. Bearing on this point, several workers have commented that manipulative contamination may run as high as 1 to 3%, while others have stated that this figure, under the most ideal of modern conditions, may run as low as 0.1 to 0.3%.

In our most recent series of sterility tests, involving 686 rolls of our own as well as cotton of competitive manufacture obtained on the open market, 16 positive tubes were recorded in 6,258 tests (i. e., one in 391, or 0.2%). This incidence of positive tubes is well below the rate to be anticipated as the result of improper manipulations and chance air-borne contamination in a well-managed aseptic area during the course of any well-conducted procedure. On the basis of these data, viewed in the light of our knowledge of manufacturing and the known shortcomings of existing testing methods, we have gained confidence in the essential universal sterility of our products and a conviction that the occasional randomly distributed contaminated culture tubes noted are due not to contamination of the product resulting from faulty sterilization methods but to inherent inadequacies in testing conditions and methods. Finally, as a further strong indication of the efficiency of present sterilization methods, it should be emphasized that never has it been possible to recover the test organism from the inoculated cotton samples that have been included in autoclave batches over a period of many years.

Thus, it is evident that the data presented by Silliker and Hess not only fail to establish a high incidence of nonsterility in market cotton, as alleged, but fail to demonstrate the existence (or even lack of existence) of unsterile packages on the market in any degree of statistical significance.

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To the Editor:—We have read the article "Sterility of Market Cotton," by John H. Silliker and Eugene P. Hess, on page 1374 of the Aug. 9, 1952, issue of THE JOURNAL. In this article the authors report their investigation of absorbent cotton sampled on the market in Los Angeles, Calif. They examined 85 packages of cotton and found by their tests that 12, or 14.2%, contained viable micro-organisms.

We have considered this report in the light of our total experience in investigation of absorbent cotton, which extends over many years, and after particular review of the reports on this phase of our work covering the past five years. Our experience and data do not support the conclusions of the authors that the present control program is not adequate to insure the consumer of the sterility of each package of market cotton. During the past five years we have examined 1,159 individual packages of U. S. P. absorbent cotton for sterility by the prescribed pharmacopeial methods. The total number of lots examined was

163. Samples from two lots were found unsterile. One of these consisted of 16 packages and the other of three packages, and all 19 packages were found to be unsterile.

We expect not only to continue our planned program for examining absorbent cotton for sterility but to include in our survey adequate samples from the output of the manufacturers investigated by the authors of the paper, as such products are available in interstate commerce.

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RABIES VACCINATION FOR POLIOMYELITIS

To the Editor:—Considerable publicity has been given recently in the lay press to the use of rabies vaccination for prophylaxis of poliomyelitis. Since rabies vaccine has the possible hazard of producing allergic encephalomyelitis in vaccinated persons, it should obviously be used only when there are proved indications. The following immunologic studies of the relationship between the poliomyelitis and rabies viruses were carried out in my laboratory.

Groups of Swiss mice were vaccinated at weekly intervals with three intraperitoneal injections (0.5 cc.) of ultraviolet irradiated poliomyelitis or rabies vaccines. The irradiated poliomyelitis and rabies vaccines were completely inactivated and prepared as previously (*J. Immunol.* **50:**317 and 331, 1945). On the 21st day after the first vaccination, the mice were given approximately 10 and 100 LD_{50} units of the Lansing strain of poliomyelitis virus or fixed rabies virus. In a series of three experiments involving over 200 mice, no evidence of cross immunity was found between the poliomyelitis and rabies viruses. In other experiments hyperimmune Lansing antiserum failed to neutralize the rabies virus and hyperimmune rabies antiserum did not neutralize the Lansing virus. On the other hand, in every experiment the vaccine or hyperimmune serum tested showed significant protection against homologous virus. These findings are contrary to recent reports in the lay press that rabies vaccination may protect man against poliomyelitis.

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REACTIONS FOLLOWING USE OF ISONIAZID

To the Editor:—Recent widespread use of isoniazid (isonicotinic acid hydrazid) and related drugs in the treatment of tuberculosis makes it appear advisable for us to mention our observation of an undesirable side-effect that heretofore has not been emphasized. This secondary symptom is the onset of dyspnea or increased severity of preexistent dyspnea while therapy with such antituberculous compounds is being maintained.

At this hospital, approximately 130 tuberculous patients have been treated with isoniazid since April, 1952, at a dose of 2 to 4 mg. per kilogram of body weight. In this group, 10% have noted onset of, or an increase in, respiratory distress. The majority of these patients had some exertional dyspnea that was due to pulmonary disease prior to the institution of such therapy. It is our belief, in retrospect, that isoniazid might have partially contributed to one death by precipitating respiratory failure. In another patient, preexisting dyspnea, which was aggravated during isoniazid therapy, failed to respond to aminophylline and oxygen and was improved only when therapy with the drug was discontinued.

Other clinicians have observed that dyspnea may occur in patients receiving these new antimicrobial compounds. While the physiological mechanism of this respiratory distress has not been adequately explained, it has been thought by some to be secondary to weight gain and increased activity (Robitzek, E. H., and Selikoff, I. J.: *Am. Rev. Tuberc.* **65:**402-428 [April] 1952). Others have postulated that there was formation of more tenacious sputum resulting in mechanical bronchiolar obstruction, which possibly contributed to dyspnea and respiratory failure (Quarterly Progress Report of Tuberculosis, V.A.-Army-Navy Study on Chemotherapy of Tuberculosis, July, 1952, p. 21). Increased weight and activity or increased tenacity of sputum was not consistently observed in all our patients receiving isoniazid who displayed some respiratory distress; however, approximately one-third of these patients did mention increased tenacity of sputum.

In conclusion, it is urged that further study be made to clarify the pathogenesis of such respiratory insufficiency. It has been necessary to discontinue isoniazid therapy in only two of our patients, and such dyspnea or increase in dyspnea subsided promptly following the discontinuance of isoniazid therapy. It is our opinion, however, that some caution is indicated when using isoniazid in any patient having marked respiratory distress.

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MEMBERSHIP IN THE BRITISH MEDICAL ASSOCIATION

To the Editor:—The secretary of the British Medical Association has informed me that a number of their members are working for oil companies in the Persian Gulf area and that there is a branch of the British Medical Association in that part of the world; in fact, it is 30 years of age.

The British Medical Association has recently decided to extend the boundaries of this branch so as to include all the territory surrounding the Persian Gulf. This branch, which will be known as the Middle East Branch of the British Medical Association, will arrange regular scientific meetings and social gatherings, mostly in Basra.

As there are a number of American physicians working around the Persian Gulf, the British Medical Association has informed me that if these physicians desire to become associate or complimentary members of the Middle East Branch they will be warmly welcomed. They should address the secretary of the branch, Prof. A. M. Critchley, Department of Public Health and Social Medicine, Royal Medical College of Baghdad, Iraq.

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VACATIONS AND DIARRHEA

To the Editor:—In The Journal, August 16, 1952, page 1475, vacations and diarrhea are editorially discussed. Reference was made to water supplies and sewage disposal systems that may become inadequate with the seasonal overloads. May I call your attention to another possibility that would seem to justify the collection of statistically significant data?

Minor diarrheal disorders may be caused by the ingestion of drinking water that is usually well tolerated by the local population. However, the visitor may be affected because of the particular type of purification method employed at the resort place or by some other active agent that is not inherent in the drinking water of his home town.

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BUREAU OF MEDICAL ECONOMIC RESEARCH

MORTALITY TRENDS IN THE UNITED STATES, 1900-1949

The monograph under this title by Frank G. Dickinson, Ph.D., and Everett L. Welker, Ph.D., Director and Associate in Mathematics of the Bureau, was recently published as Bulletin 92 of the Bureau of Medical Economic Research of the American Medical Association. The article below summarizes the bulletin's 29 pages, 11 tables, and 11 charts.—Ed.

The decline in the crude mortality rate from 17.2 deaths per 1,000 population in 1900 to 9.7 in 1949 understates the health progress of the last half century. While the population has doubled, the number of persons over 65 has quadrupled in this period. A significant gain in life expectancy, even in late middle age, has resulted from the mortality rate reductions between 1900 and 1949. Life expectancy at birth was recently estimated at 47.3 years for 1900. By 1949 it had risen to 67.6 years. These life expectancy figures are based on the mortality experience of the persons at each age in that calendar year. Thus life expectancy at birth probably understated the average age at death, as improving health conditions lengthen the actual life period. The average age at death of babies born in a given calendar year cannot be computed until all have died—roughly, a century later. A generation life table could then be computed, but it would be outmoded long before it was completed. Life expectancy at birth is not a forecast, although forecasters use it. It is a statement of the experience of persons at all ages under the health conditions of the given calendar year.

Life expectancy decreased almost linearly from age 5 to age 50 in 1901 and from age 1 to age 50 in 1949. From age 50 to age 75 life expectancy decreased at a decreasing rate. From age 5 to age 25 the gains from 1901 to 1949 in life expectancy for white males were about the same on a percentage basis, ranging from a low of 16.0% at age 10 to a high of 16.8% at age 20. The percentage gain dropped at a uniform rate from 16.1% at age 25 to 8.7% at age 50. The decline in the percentage gain continued to 7.8% at age 65, but above that age it rose again to 10.3% at age 75. At both age 45 and age 75 the gains were 10.3%, while between these two ages they were less; below age 45 the percentage gains were more than 10.3%. Is not the equality of percentage gains in life expectancy at ages 45 and 75 indicative of considerable success at the high ages? Life expectancy is now very near "three score years and ten" at 67.6 years in 1949 (over 70 for all females and 71 for white females). It is a generally accepted hypothesis that this trend cannot continue indefinitely, unless some great new factor appears. As yet no maximum is in sight.

The mortality rate decrease at pre-kindergarten ages represents 50% of the gain in life expectancy since 1901; 23% of the increase represents the gains at ages 5 to 30; 24% is included for ages 31 to 65; and only 3% occurs after age 65. It would be totally unrealistic to expect the mortality gains at the later ages to rival those at the earlier ones, particularly percentagewise. To date the most effective control and curative procedures have been established for the "younger" causes of death. In 1900 the death rate for pneumonia (including influenza) was 202.2 (deaths per 100,000 population). In 1948 it had declined to 38.7.

A comparison of mortality by age groups for the death-registration states for 1900 and 1949 reveals rate reductions for each age class as well as for "all ages." Significant gains have been recorded at all ages; for example, the decline was 22% for the age group 65 to 74. The greatest reduction occurred in the 1 to 4 year age group. The decline has been steady except for the time of the 1918 influenza epidemic and random fluctuations. With the low rate of 1.5 per 1,000 for 1949 the trend for this group has started to approach a horizontal line. At the higher ages the decline during the half century came mostly during the last decade and a half.

The rate reductions were higher and the percentage reductions lower in the higher age groups. The six age groups from 5 years to 64 years exhibit similar trends over the last half century, affected by random fluctuations and the 1918 epidemic. The age group 65 to 74 exhibits the same trend, although it is subject to more violent fluctuations than the rates for the 5 to 64 age groups. The downward trend was established by 1929. Beyond age 75, the 75 to 84 year age group reflects even greater fluctuations, and its downward trend did not begin until 1936. For the 85 and over group the record is confusing and no definite trend has been established. The changing age distribution of this open-end group may make any trend almost meaningless.

The tuberculosis mortality rate dropped from 194.4 in 1900 to 30.0 in 1948. In contrast, heart and cancer rates have increased in importance from 137.4 and 64.0 in 1900 to 322.7 and 134.9 in 1948. These increases are partially explained by the fact that persons who do not die from tuberculosis or childhood diseases (many of which have literally vanished) live to become cancer and heart victims. The leading causes of death in order of increasing average age at death were accidents, tuberculosis, pneumonia, cancer, diabetes, nephritis, heart, and cerebrovascular (the oldest). The three "youngest" causes in 1948, accidents, tuberculosis and pneumonia did not cause deaths at ages that are really "young." Accident victims were 46.5 years old on the average; tuberculosis deaths occurred at an average age of 47.0 years. Pneumonia is peculiar in its age distribution; although the average age of its victims was 48.1 years, it is more properly thought of as two causes since it is of importance for the very old and very young and of minor significance for the middle-aged.

The average age at death is one of the simplest indexes of the changing death problem. In 1900 deaths occurred at an average age of 36.9 years. By 1948 this had been raised to 58.6 years, a gain of 21.7 years, or almost 60%. This resulted from changes in the average age at death and the relative number of deaths attributable to each cause. The authors consider standardized death rates too misleading to use.

In number of deaths, heart disease ranked first in 1948 with 32.6%. Cancer, the second most important cause, was responsible for 13.6%. In contrast, in 1900 pneumonia, the leading killer, accounted for 12.9% of all deaths, less than cancer in 1948. Tuberculosis was a close second with 10.4%. Heart was third with 8.5%. "All other" causes—other than the leading seven—accounted for 49.6% of all deaths in 1900. Heart and cancer alone were responsible for 46.2% in 1948. "All other" causes were responsible for only 25.6% of all deaths in 1948. The lead of the seven leading causes increased sharply.

This changing pattern of deaths has no doubt had considerable effect on the practice of medicine. In 1900 the doctor attending a patient in his final illness might be fighting any one of a number of maladies. In 1948 in one case in three he was dealing with heart disease and in almost one-half of the cases with either heart disease or cancer. Did this change encourage specialization by physicians? Certainly the need for broad training overshadowed the need for specialization in 1900.

Greater emphasis has usually been placed on numbers of deaths and therefore on the "older" causes of death. The use of life years lost and working years lost changes the ranking of the various causes. These two measures emphasize the importance of accidents. While heart disease accounted for 32.6% of all deaths, 19.9% of all life years lost, and 12.7% of all working years lost, accidents were responsible for 6.8% of the deaths, 10.0% of life years lost, and 13.3% of the working years lost in 1948. Thus, heart disease ranks first in number of deaths and life years lost, but accidents hold first in working years lost.

The relative number of deaths today at the lower ages is much less than in 1900. The only exception to this generality is pneumonia (and influenza), which has risen from 18% to 22.9% for the "under 1" group. In 1900 almost 30% of the deaths occurred prior to age 5; in 1948, only 9%. At age 75 or above 12.8% of the deaths occurred in 1900. The 1948 figure had increased to 27.6%.

A general summary of the situation is given by the percentage distributions for the three "younger" causes and the four "older" causes in 1900 and 1948. In 1900 the three "younger" causes exhibited a bimodal character, with peak percentages of 10.4 for the "under 1" group and 9.7 for the age group 1 to 4, a total for the two groups of 20.1% of all deaths. There was another relative peak of 16.2% for the age group 25 to 34. By 1948 the percentage for deaths under age 5 had dropped to only 12.8, one of two peaks; the other was 12.9% for the age group 65 to 74. Thus

the "younger" causes had aged materially. The distributions for the two years for the four "older" causes showed the same aging process. In both 1900 and 1948 the peak occurred in the 65 to 74 age group, but deaths were concentrated more closely in 1948 about the modal class.

While the causes of death were all "aging" and the average age at death had risen to 58.6 years by 1948, the median age at death had risen from 36.7 years in 1900 (for the registration area) to 65.2 in 1948 (a rise of 78%). Average age at death is greatly influenced by the age distribution of the population. Immigration and changes in the birth rate can change the age distribution. In the future we can expect aging in the causes of death in two ways. Average ages at death can rise, although there probably is a practical upper limit; and, when this limit is approached, persons will die at ages nearer the mean or median age at death.

In view of the great reduction in the last half century in the general mortality rate, in the mortality rates in each separate age group for all causes combined, and the reduction in mortality rates in many age groups for some causes, it is startling to find that some 1948 rates exceeded those for 1900: for cancer in every age group, for diabetes for all ages from 45 on, and for heart disease at all ages above 35. It is often suggested that many of these rate increases are due to improved diagnosis. Death certification has improved, and physicians are using fewer ill-defined causes. It is hardly possible, however, to attribute all the rise in these age-cause specific mortality rates to these factors.

If the number of deaths per thousand illnesses for a given disease is decreasing, then the number of survivors, whose lives are probably impaired, is increasing. The higher death rate from diabetes at age 45 and over is an excellent example. The effect of the survival of persons with impairments has raised life expectancy at birth and at the younger ages, but not necessarily life expectancy at the higher ages. It is entirely possible that an increased number of persons with impairments will decrease life expectancy at the higher ages in the future. It has been observed that absolute and relative increases in life expectancy are smaller the higher the age; and a possible eventual decrease is by no means inconsistent with these trends.

The extent of impairments in our population is not known. Apparently the gains in knowledge of preventive and curative techniques have occurred so rapidly that they have overcome most of the adverse effects of the increased numbers of persons with impairments. There are always some of such persons in any population. Our morbidity records are inadequate to determine whether the percentage has generally increased or decreased since 1900.

Infant and maternal mortality have served traditionally as indexes of the general health situation. The annual number of maternal and infant deaths has been, however, far fewer than deaths from heart disease and cancer. Birth registration began formally in the United States in 1915. In that year there were 99.9 infant deaths and 6.1 maternal deaths per 1,000 live births in the death-registration states. In 1933 when all the states were first included in the birth registration area, there were 58.1 infant and 6.2 maternal deaths for each thousand live births. The rates dropped to 29.1 infant deaths and 0.8 maternal deaths in 1950, one-half the 1933 infant rate and a little over one-eighth the 1933 maternal rate. A 1951 maternal mortality rate of 0.1 deaths per 1,000 live births has been attained by two states. The problems of maternal mortality have become local in nature, and we suggest the discontinuance of this series by the National Office of Vital Statistics.

In the case of infant mortality, a time and not a cause of death, premature births and anatomic anomalies of a few of the live born seem to put a floor under the rate. The practical limit may be near the present level. Medical care, however, has reduced deaths during most of the first year, and the authors believe that the first month of life should be emphasized. The infant mortality rate should be discontinued, and a neonatal rate for the first month of life should be substituted by the National Office of Vital Statistics. In the future a one week period may be satisfactory. Since infant mortality is based on age at death, the change in the series would not reduce the published information on the causes of death. These suggestions regarding the omission from future publication of maternal and (12 months) infant mortality rates clearly mark the end of an era of remarkable reductions in mortality.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

FEE SPLITTING AND THE INCOME TAX LAW

The Income Tax Division of the Bureau of Internal Revenue recently handed down an opinion on two questions of interest to physicians: whether for federal income tax purposes payments made by surgeons to other physicians (1) for professional assistance and (2) under fee-splitting arrangements are deductible as ordinary and necessary expenses.

With respect to the payments for professional assistance, the opinion concluded that reasonable compensation paid by a surgeon for personal services actually rendered may be deducted as ordinary and necessary expense of carrying on a trade or business, including a profession. As to payments made under fee-splitting arrangements, the opinion held that whether reasonable payments made by a surgeon, on a split-fee basis, to another physician who refers patients to him represent a deductible expense must be determined in the light of all the circumstances in each case. As a general rule, it was stated in the opinion, such payments are deductible provided they are normal, usual, and customary in the profession and in the community; are appropriate and helpful in obtaining business; and do not frustrate sharply defined national or state policies evidenced by a governmental declaration proscribing particular types of conduct.

Physicians should note well the conditions under which payments on a split-fee basis are deductible. They should also understand clearly that this opinion does not make ethical a course of conduct declared to be unethical by the Principles of Medical Ethics.

MEDICAL MOTION PICTURES

The Suction Socket Artificial Limb: 16 mm., color, sound, showing time 21 minutes. Produced in 1951 by the Presentation Division, Veterans Administration. Procurable on loan from Central Office Film Library, Motion Picture Service, Office of Information, U. S. Department of Agriculture, Washington 25, D. C.

This film illustrates the use, application, and advantages of a suction socket artificial limb. The film also shows the fitting, the principles, and the treatment by the physiatrist to develop muscle, particularly in the stump. Included in this demonstration is a discussion of some of the contraindications for its use. For those cases where it is indicated, it shows great advantage over the artificial limb with the pelvic balance. It shows ability to rotate well at the hip joint and also slightly at the knee joint. A more normal gait is simulated. The film is recommended for orthopedic surgeons and general practitioners. It is also suitable for residents in orthopedic surgery, interns, physical therapists, and makers of prostheses. The photography is well done.

Back Pressure Arm Lift Method of Artificial Respiration: 16 mm., black and white, sound, showing time 9 minutes. Produced in 1952 by and procurable on purchase ($37.50) from Seminar Films, Inc., 347 Madison Ave., New York 17.

This film is a demonstration of the newly adopted back pressure arm lift method of artificial respiration, which supersedes the Schaefer system. The approved method is illustrated in the prescribed manner. It is not an explanation of why the method is preferred, nor does it present any of the alternatives or modifications that can be used under unusual circumstances, such as in the case of a broken arm.

The film will be a good aid for teaching lay audiences, but it is inadequate for medical or highly trained personnel. Anyone using it will have to be prepared to answer questions not answered in the film. The photography and narration are satisfactory.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Indust. Hyg. & Occup. Med., Chicago

5:517-606 (June) 1952

Rational Approach to Air-Pollution Legislation. G. E. Best.—p. 517.
Deposition of Siliceous Dust in Lungs of Inhabitants of Saharan Regions. A. Policard and A. Collet.—p. 527.
Quest for Suspected Industrial Carcinogen. C. S. Weil, H. F. Smyth Jr. and T. W. Nale.—p. 535.
Organization and Operation of Study of Air Pollution in Relation to Experimental Carcinogenesis. P. Kotin.—p. 548.
Clinical Pulmonary Physiology. 1. Evaluation of Function Impairment and New Developments in Therapy of Chronic Pulmonary Disease. H. L. Motley.—p. 554.
Vapor Toxicity of Tetrachloroethylene for Laboratory Animals and Human Subjects. V. K. Rowe, D. D. McCollister, H. C. Spencer and others.—p. 566.
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American Journal of Pathology, Ann Arbor, Mich.

28:321-572 (May-June) 1952

Thymic Tumors Characterized by Lymphangioendothelial Structure. D. S. Hubbell and A. A. Liebow.—p. 321.
Spontaneous Demyelinating Disease of Adult Rats. A. M. Pappenheimer. —p. 347.
Study of Glioblastoma Multiforme by Golgi Method. I. Klatzo.—p. 357.
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Dissolution of Fatty Cysts in Precirrhotic and Cirrhotic Livers of Choline-Deficient Rats Treated with Lipotropic Factors. W. S. Hartroft and E. A. Sellers.—p. 387.
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Pathogenesis of Atheroma. N. G. B. McLetchie.—p. 413.
*Myocarditis, Arteritis, and Focal Hepatic, Splenic, and Renal Granulomas Apparently Due to Penicillin Sensitivity. D. Waugh.—p. 437.
Nature of Agenesis and Deficiency of Parts. Influence of Intrinsic Factors in Disease When Development of Body is Abnormal, Illustrated by Agenesis of Digits, Facial Hemiatrophy, and Cerebral Agyria and Microgyria. K. Inglis.—p. 449.
Comparative Morphogenesis of Dermo-Epidermal Nevi and Malignant Melanoma. S. W. Berkheiser and A. E. Rappoport.—p. 477.
Observations on Persistence of Hepatic Glycogen After Death. T. G. Morrione and H. L. Mamelok.—p. 497.

Granulomas Due to Penicillin Sensitivity.—A patient developed clinical hypersensitivity to penicillin and died suddenly a short time later. At necropsy the principal findings were diffuse interstitial myocarditis, acute and subacute arteritis, and granulomatous lesions in the liver, spleen, and kidneys that were similar to those seen in cases of sulfonamide sensitivity. There was ample indirect evidence of sensitivity to penicillin. Prior to the second course of treatment, the blood contained a normal number of eosinophils. During therapy there was a rapid and marked eosinophilia, coinciding with the appearance of an erythematous skin eruption. When these manifestations appeared, penicillin was the only drug being given other than insulin. Since insulin therapy had been continuous, it is unlikely to have been the cause of such a reaction of hypersensitivity. In addition to these clinical evidences of allergy, the visceral lesions were of the type seen in other hypersensitive states. Of special interest is the intense interstitial myocarditis that is assumed to have caused death.

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Titles marked with an asterisk (*) are abstracted.

American Journal of Surgery, New York

83:721-838 (June) 1952

Stenosed Arteriopathy of Hunter Canal and Loop of Adductor Magnus. E. C. Palma.—p. 723.
*Combined Operations in Management of Cancer in Head and Neck. J. O. Vieta and J. E. Mulé.—p. 734.
Recent Advances in Management of Burns. C. W. McLaughlin Jr. and D. K. Neis.—p. 746.
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Femoral Hernia, with Special References to Its Complications. D. B. Pfeiffer and F. D. Sain.—p. 767.
*Acute Appendicitis in Chronically Ill Geriatric Patients. L. Carp and J. A. Arminio.—p. 773.
*Is the Reflux of Bile into the Pancreatic Ducts a Normal or Abnormal Physiologic Process? N. F. Hicken and A. J. McAllister.—p. 781.
Familial Incidence in Polycystic Kidney Disease: Report of Three Cases. E. J. Adlerman.—p. 787.
Intestinal Obstruction. C. H. Lupton.—p. 794.

Cancer in the Head and Neck.—Of 91 patients with cancer in the head and neck reviewed for operative treatment, 26 were considered inoperable and 65 were considered operable. Of the 65, 37 were treated by stages (radiotherapy plus surgery or surgery in stages), 3 refused treatment, and 25 were treated with a one-stage combined operation, including excision of the primary lesion and the node-bearing areas. With the present continued delay in early diagnosis of cancer of the head and neck, therapy should be more aggressive if a greater number of patients are to be saved. The concept of excision and dissection in continuity is not new. However, it should be performed earlier and more frequently. The plea is not for more extensive surgery; it is rather for adequate surgery. Such well-conceived operations should be planned and performed by surgeons experienced in the treatment of extensive cancer. Surgery performed with good judgment and modern preoperative and postoperative care offers patients with advanced cancer of the head and neck more than irradiation therapy. Nine cases of carcinoma (one of the lip, one of gingiva and floor of mouth, two of the tongue, one of the salivary glands, one of the thyroid gland, two of the larynx, and one of the skin of the face with metastases to the left submaxillary lymph nodes) are described as examples of this plan of treatment used either for cure or palliation. Their management likewise showed that cryptic regional lymph node metastases may be demonstrated with certainty by dissecting the nodes in continuity, when possible, with the primary growth. Although nonsurgical methods of palliation in the treatment of cancer may be developed, surgery offers an excellent means to give relief of pain, remove foul necrotic ulcerations, and establish airways and oral feedings for patients with overwhelming localized cancer in the head and neck.

Acute Appendicitis in Geriatric Patients.—Of 21 chronically ill poor risk geriatric patients with acute appendicitis observed between 1939 and 1951, 10 had perforations. Five of these had peritonitis and died after appendectomy and drainage (a mortality rate of 23.8%). The other five had an abscess. In two of these drainage alone was done. They survived and did not require further surgical treatment. Appendectomy was performed on the remaining 11 patients who did not have perforations, with no mortality. Appendicitis is infrequent in geriatric patients and usually serious. Atypical clinical syndromes, difficulty in diagnosis, delayed surgical intervention, catharsis, and accompanying degenerative disease all contribute to a high mortality. Mortality statistics from other sources are also high. Peritonitis, pneumonia, cardiac failure, and thrombosis were the leading causes of death, as revealed by necropsies in two of the authors' cases and in 18 cases collected from the literature. Microscopic studies were made of acutely inflamed appendices and of others removed in necropsies on patients aged 60 and over who died of causes other than acute appendicitis. The observations suggested that early massive gangrene might result from diminution or ab-

sence of lymphoid follicles in the wall of the appendix, sclerosis of the vessels supplying it, obstruction in its lumen, and previous damage to the appendix by inflammation. The authors do not subscribe to the so-called conservative treatment in which the appendix is not removed or in which abscesses or peritonitis are not drained. Antibiotic therapy has supplemental rather than substitutional value for surgery. Appendectomy is indicated except in cases in which technical difficulty would prolong the operative time to such an extent that the hazard to life would be pronouncedly increased or when additional trauma would be instrumental in further spread of infection. Generally, the McBurney incision is preferred.

Reflux of Bile into Pancreatic Ducts.—In 100 patients, 75 of whom were operated on for cholelithiasis and 25 for choledocholithiasis, the pancreatic and bile ducts were visualized by operative and postoperative cholangiography, accomplished by injecting a solution of iodopyracet (diodrast®) directly into the gallbladder and bile ducts. Three distinct anatomic arrangements were observed, as follows: The common bile duct and the pancreatic duct (the duct of Wirsung) formed a common ampullary channel in 30 patients; in 57 patients they both opened into the duodenum through a shallow duodenal papilla, and in 13 the ductal systems had separate duodenal orifices. In all three varieties the contrast fluid was seen to flow into the pancreatic duct; therefore, one must assume that the reflux phenomenon occurs despite of the anatomic arrangement of the terminal portion of these ducts. This is contrary to the "open channel" theory that has been accepted previously. It is commonly believed that cholecystopathies and the reflux of bile are precursors of acute pancreatitis. Only 3 of the 100 patients who had biliary tract disease and associated pancreatic reflux had acute or subacute pancreatitis as demonstrated by routine biopsies of the uncinate process of the pancreas. Apparently the reflux of bile into the pancreatic ducts is a normal physiological process and seldom produces inflammatory changes within the pancreas.

Annals of Surgery, Philadelphia

135:755-944 (June) 1952

*Early Results Following Therapeutic Ligation of Hepatic Artery: Preliminary Report of Cases. A. I. Chenoweth.—p. 756.

Massive Hemangiomas of Liver. H. Wilson and W. T. Tyson Jr.—p. 765.

*Theories on Treatment of Breast Cancer and Observations on Its Natural Course. W. D. Gatch and C. G. Culbertson.—p. 775.

Endocrine Relationships in Benign Lesions of Breast. L. C. Kier, R. C. Hickey, W. C. Keettel and N. A. Womack.—p. 782.

Clinical Significance of Blood Volume Determinations. W. H. Parsons, W. T. Williams and L. J. Forsythe.—p. 791.

Fluid and Electrolyte Requirements in Severe Burns. E. I. Evans, O. J. Purnell, P. W. Robinett and others.—p. 804.

Adenomatous Polyps of Colon and Rectum. W. R. Sandusky and J. R. Parsons Jr.—p. 818.

Volvulus of Sigmoid Colon. G. O. Dean and J. W. Murry.—p. 830.

Cancer of Rectum: Study of Long-Term Survival. F. A. Coller, R. H. Lillie, M. F. Bryant Jr. and W. E. Brown III.—p. 841.

Construction of Rectal Sphincter and Restoration of Anal Continence by Transplanting Gracilis Muscle: Report of Four Cases in Children. K. L. Pickrell, T. R. Broadbent, F. W. Masters and J. T. Metzger.—p. 853.

Abdominal Emergencies Following Unrelated Surgical Procedures. R. S. Sparkman.—p. 863.

Hernia in Linea Semilunaris. A. R. Koontz.—p. 875.

Treatment of Congenital Inguinal Hernia. J. W. Duckett.—p. 879.

*Indications for Operation in Disc Lesions in Lumbosacral Spine. J. A. Key.—p. 886.

Subjective and Objective Criteria in Diagnosis of Meningiomas of Brain, with Remarks as to Mortality and Useful Survival. G. Horrax and R. E. Strain.—p. 892.

Degrees of Recovery Following Prolonged Post-Traumatic Coma. E. Campbell and R. D. Whitfield.—p. 899.

Direct Measurement of Intravascular Pressure in Components of Circle of Willis: Contribution to Surgery of Congenital Cerebral Aneurysms and Vascular Anomalies of Brain. B. Woodhall, G. L. Odom, B. M. Bloor and J. Golden.—p. 911.

Influence of Normal Serum, Its Derivatives, and of "Wound Healing Agents" on Human Epidermis in Vitro. M. Allgöwer, C. M. Pomerat and T. G. Blocker Jr.—p. 923.

Therapeutic Ligation of the Hepatic Artery.—Experimental observations collected from the literature provide the following rationale for therapeutic ligation of the hepatic artery in cirrhosis of the liver: There are at least two factors in the production of portal hypertension, (1) decrease in the available portal bed, and (2) increase in the arterial bed, probably with associated abnormally large arteriovenous communications within the liver substance. Good results were obtained in the first six patients who were subjected to ligation of the hepatic artery for control of ascites or hemorrhage and who were reported by Rienhoff in 1951. A short time after this report, the author utilized this procedure for control of massive hemorrhage from esophageal varices in two desperately ill patients, a 38-year-old man and a 43-year-old woman. While Rienhoff ligated the common hepatic artery distal to the gastroduodenal branch, the author's decision to ligate near the celiac artery was based on the presence in both patients of a vigorous, machinery-like thrill along the entire course of the hepatic artery, accompanied by an audible bruit in the epigastrium of the second patient. This bruit may be significant in portal hypertension. The procedure as carried out in these patients was not technically easy. Access to and exposure of the main trunk of the common hepatic artery was difficult through the abdominal incision and only slightly less so through the thoracoabdominal approach. If, therefore, ligation of the vessel in the region of the common duct provides the same end result, that is the desirable site, for it is much more accessible. The splenic artery was also ligated in the second patient, but was not ligated in the first patient, whose spleen was not enlarged. The wisdom of this decision remains in doubt, as it depends in part on the rationale of the ligation procedure. Although the mechanical factor of portal hypertension has been emphasized in discussion of hepatic artery ligation, it seems quite likely that a physiological alteration results from the increased portal flow attendant on the diminished arterial flow. The author believes that hepatic artery ligation may prove to have merit, but additional information, both experimental and clinical, is needed to clarify the complex physiological process involved. Until such information is available, the procedure should be used only in carefully selected patients on whom intensive follow-up studies can be made.

Treatment of Cancer of Breast.—The authors examined two concepts that have governed the treatment of cancer of the breast: (*a*) that it spreads entirely or almost entirely by way of lymphatics, and (*b*) that the earlier surgical treatment is instituted the better is the chance of cure. They showed that breast cancer spreads by way of blood vessels in many and possibly in all cases. When it has invaded lymph nodes, it is widespread in lymph vessels around them, so that all the vessels must be removed with the nodes to eradicate the growth. It seems doubtful that this is often achieved. Tissue resistance to the growth of breast cancer is very great, and heretofore it was not fully realized how much the tissue does to destroy or to retard the growth of bits of cancer not removed at operation. Since operation is likely to be done sooner for rapidly growing cancers than for those of slow growth, the results of early operation may actually be statistically poorer than the results of delayed operation. This does not mean that early operation is worse for the individual patient. The authors believe that the fate of the patient depends chiefly on the success of her body in opposing the growth of cancer. In some normal-appearing breasts, cancers of microscopic size can be demonstrated, and the authors infer that these little growths may take a long time to grow large enough to be palpable and may also metastasize. Perhaps spontaneous cure of breast cancer is not infrequent. Tissue resistance sufficient to arrest its growth for many years may sometimes destroy the cancer. Although the theories on which the Halsted operation is based are no longer tenable, this operation is still the best treatment available for most cases of cancer of the breast. Its use is now justified not by theory but by experience. The procedure keeps a considerable number of patients with operable growths free for five years or longer of any apparent persistence of cancer and about 85% die of intercurrent disease or internal metastases without an external growth. The good results observed after this operation when axillary metastases are present are probably due to tissue resistance to cancer growth and not to removal of every bit of cancerous tissue. If the surgeon leaves too much cancerous tissue or inflicts too much damage on the tissues, he may defeat the efforts of nature to help him.

Disk Lesions in Lumbosacral Spine.—Evidence showed that in most cases the pain caused by a disk lesion in the lumbosacral spine will eventually subside, with or without treatment. This is especially true of early cases in which the symptoms are not severe. On the other hand, operative removal of the disk is a relatively safe procedure, is followed by a short convalescence, and offers an acceptable chance that the patient will obtain prompt relief. The decision whether or not to operate on a disk lesion is based on the persistence and severity of pain and disability and the patient's reaction to these symptoms rather than on any typical physical or laboratory findings. Except in unusual cases in which the pain is very severe and resistant to all forms of conservative treatment, or in cases in which the patient has had previous severe attacks, the author rarely advises operation for a disk lesion unless the pain has persisted for four weeks or longer despite conservative treatment. Then the operation may be advised, but is not urged, and the decision whether or not to operate is a matter for discussion between the surgeon and the patient. A myelogram is rarely done until operation is decided on; it is then useful in localizing the lesion or in diagnosing occasional atypical cases, but is rarely the decisive factor in deciding on surgical intervention.

Diseases of Chest, Chicago

21:613-728 (June) 1952

Symposium on ACTH and Cortisone in Diseases of Chest. E. R. Levine. —p. 613.
*Precordial Migraine. J. F. Briggs and J. Bellomo.—p. 635.
Primary Carcinoma of Lung. S. A. Gittens and J. P. Mihaly.—p. 641.
*Alveolar Cell Tumor of Lung. J. N. White, G. F. Madding and L. R. Hershberger.—p. 655.
Treatment of Spontaneous Pneumothorax by Means of Continuous Intrapleural Suction. F. L. Kreutzer, L. G. Brizzolara and W. L. Rogers. —p. 663.
Hemoptysis, Its Significance and Methods of Study. E. F. Parker.—p. 677.
Pulmonary Fibrosis in Generalized Scleroderma: Report of Case and Review of Literature. L. D. Hayman and R. E. Hunt.—p. 691.

Precordial Migraine.—The term migraine is usually applied to the periodic, recurring type of headache, often associated with gastrointestinal and ocular symptoms, which frequently has a hereditary and familial tendency. The head pain may be so severe that it overshadows associated symptoms; on the other hand, the patient may have violent distress in various organs of the body with the head pain absent or so slight that he disregards it. This results in what is termed a migraine equivalent. In this paper the authors are concerned chiefly with precordial migraine. After briefly reviewing the previous literature on this migraine equivalent, they say that 159 of 684 patients with migraine had symptoms suggesting the presence of precordial types of migraine. Palpitation occurred in 83, simple tachycardia in 14, and paroxysmal tachycardia in 3. Nondescript types of chest pain occurred in 92 and a rather definite type of anginal pain in 37. When the precordial distress occurs in conjunction with an attack of cephalalgia, the true nature of the chest distress is usually recognized. However, when the precordial pain or distress occurs as a migraine equivalent, failure to recognize it as such often leads to erroneous diagnosis of organic heart disease. To avoid such an erroneous diagnosis and establish that the precordial symptoms are a migraine equivalent, the patient's history should be investigated for attacks of precordial symptoms concurring with cephalalgia or with other disturbances likely to represent a migraine equivalent.

Alveolar Cell Tumor of Lung.—Alveolar cell tumors of the lung are rare and the symptoms are often atypical and misleading. The tumors may be nodular, miliary, diffuse, or pneumonic. The case reported in this paper is noteworthy because the lesion persisted for about 11 years before death ensued. Although the patient was seen throughout this period by a number of physicians, the most frequent diagnosis was unresolved pneumonia. Congenital atelectasis with pneumonitis and carcinoma were considered at the time of his hospitalization in 1946, about four years before his death. The chief symptom was productive cough. Surgical excision of the right middle lobe and subsequent x-ray therapy produced considerable palliation. The authors feel that this was a pneumonic type of alveolar cell carcinoma. This is another example of how closely carcinoma of the lung can simulate both clinically and roentgenographically other pulmonary lesions. It also demonstrates the fallacy of waiting, watching, and taking frequent roentgenograms. Had this lesion been more localized at the time of exploration, cure might have been possible. Excision is the treatment of choice, but roentgen therapy is of aid in inoperable cases. Metastases usually occur only to regional lymph nodes. In the case presented, distant metastases were also found.

Electroencephalography and Clin. Neurophys., Boston

4:141-260 (May) 1952

Response of Experimental Epileptic Foci to Intravenous and Topical Metrazol. H. C. Johnson and A. E. Walker.—p. 131.
Effect on Electrical Activity of Brain of Intra-Arterially and Intra-Cerebrally Injected Convulsant and Sedative Drugs (Metrazol and Nembutal). K. Shimizu, S. Refsum and F. A. Gibbs.—p. 141.
Paroxysmal High Voltage Discharges from Isolated and Partially Isolated Human and Animal Cerebral Cortex. F. A. Echlin, V. Arnett and J. Zoll.—p. 147.
EEG Findings in 18 Patients with Brain Abscess: Case Reports and Review of Literature. I. Pine, T. H. Atoynatan and G. Margolis. —p. 165.
EEG Findings in Certain Type of Psychosomatic Headache: Dysrhythmic Migraine. A. A. Weil.—p. 181.
Relation of Human Electromyogram to Muscular Tension. V. T. Inman, H. J. Ralston, J. B. de C. M. Saunders and others.—p. 187.
Influence of Sleep on Focal Slow Wave Activity: Correlation with Epileptogenic and Non-Epileptogenic Lesions. C. Grossman, L. M. Golub and J. K. Merlis.—p. 195.
Crosscorrelation and Autocorrelation Studies of Electroencephalographic Potentials. M. A. B. Brazier and J. U. Casby.—p. 201.

Gastroenterology, Baltimore

21:1-184 (May) 1952

Present Status of Exfoliative Cytology in Diagnosis of Gastrointestinal Malignancy. C. E. Rubin, W. L. Palmer and J. B. Kirsner.—p. 1.
*Histology of Normal Gastric Mucosa: Investigation into State of Normalcy of Stomachs of Persons Without Upper Gastrointestinal Complaints. E. D. Palmer.—p. 12.
The Pancreas: Contributions of Clinical Interest in 1950. R. Elman and Z. H. Lieberman.—p. 24.
Pedigree of Family with Hereditary Chronic Relapsing Pancreatitis. M. W. Comfort and A. G. Steinberg.—p. 54.
Water and Electrolyte Excretion of Human Pancreas. J. A. Hildes, M. H. Ferguson and L. C. Bartlett.—p. 64.
Combined Service Approach in Treatment of Bleeding Peptic Ulcer. W. L. Alsobrook, M. W. Schell and R. S. McCleery.—p. 71.
Measurements of Disappearance of Radioactive Tagged Albumin from Serum and Excretion of I^{131} in Urine of Patients with Cirrhosis. M. P. Tyor, J. K. Aikawa and D. Cayer.—p. 79.
Study of New Quarternary Ammonium Derivative, Prantal, Capable of Reducing Gastric Secretions and Motility; Tests in Animals and Man, Trial in 44 Patients with Peptic Ulcer. C. R. Rowe Jr., K. S. Grimson and B. H. Flowe.—p. 90.
Incidence of Gallbladder Disease in Chronic Hemolytic Anemia (Spherocytosis). G. C. Bates and C. H. Brown.—p. 104.
Enteritis Necroticans. M. Patterson and H. D. Rosenbaum.—p. 110.
Diverticulitis of Sigmoid Colon. F. J. McGowan and W. I. Wolff. —p. 119.
*Results of Treatment of Ulcerative Colitis with Salicylazosulfapyridine. L. M. Morrison.—p. 133.
Suppression of Intestinal Flora in Man by Means of Mixtures of Poorly Absorbed Antibiotics. E. Jawetz and H. R. Bierman.—p. 139.

Structure of Normal Gastric Mucosa.—An examination was made of mucosal specimens removed after an eight hour fast from the stomachs of 105 "normal" controls between the ages of 18 and 67. These specimens were taken with the vacuum tube biopsy instrument from the anterior wall, close to the greater curvature, in a line with the axis of the esophagus. Tissue removed by this method, unlike surgical and necropsy material, is believed to be largely free of artefacts. The muscular mucosa was normal in all instances, except for minor round cell infiltration in three. There was no muscle fragmentation. Although smooth muscle tissue could be traced between the glands in all specimens, it caused no distortion of the mucosal architecture. The glands of all sections were uniformly straight and empty of formed elements. Simple retention cysts were observed in five. There were no abnormalities of gland cell make-up, and no intestinal metaplasia was found. The interstitial tissue of the glandular layer was notably sparse in 91 specimens. In the others there was either minor focal edema, scattered aggregations of round cells, more diffuse round cell infiltration, or occasional large foci of lymphocytes. The interstitial tissue of the foveolar layer showed similar minor changes in 24 instances.

The neck layer, referring to those cells of the tubule that join the gland and the bottom of the foveola, is believed to be the most vulnerable region of the mucosa; it was entirely normal in 103 specimens. One instance of focal necrobiosis and one of coagulation necrosis were observed. The foveolae were normal in all specimens. In 11 they contained either migrating cells or cell casts. No abnormalities of the surface epithelium were observed. It is concluded that the gastric mucosa of the healthy adult is normally uniform microscopically. There was no indication that evidence of injury and repair, of chronic inflammation, and, in particular, of the chronic gastritides can in any sense be considered "physiological" or "normal" in the human stomach.

Salicylazosulfapyridine in Ulcerative Colitis.—Results of treatment with salicylazosulfapyridine for two and a half years are reported in 52 patients between the ages of 16 and 58 who had chronic nonspecific ulcerative colitis. The drug was administered in doses of 1.5 gm. every three hours during the waking hours for two weeks. Following a rest of two weeks the course was repeated once or twice when indicated by the response of the patient. Thirty patients were improved, 8 had to discontinue treatment because of hypersensitivity to the drug manifested by nausea, pains in the joints, and mild secondary anemia, 2 had to reduce it to such small doses for tolerance that its effect became doubtful, and 12 were therapeutic failures. In the 30 patients in whom improvement was either temporary or maintained, the favorable response was manifested by disappearance or reduction of abdominal pains or of the diarrhea or blood in the stools, the reduction or restoration of temperature to normal, and the reduction or disappearance of toxic symptoms associated with the disease. Salicylazosulfapyridine may be a useful drug in the treatment of chronic ulcerative colitis when used carefully and with the realization of its limitations. Further studies are suggested to develop a better tolerated, more effective compound related to salicylazosulfapyridine for treatment of chronic ulcerative colitis.

Industrial Medicine and Surgery, Chicago

21:251-310 (June) 1952

Clinical Orientation to Alcoholism. R. G. Bell.—p. 251.
Industrial Medical Practice—1952. R. F. Buchan.—p. 261.
Psychosomatic Principles of Nutritional Therapy. H. T. Kelly.—p. 266.
The Industrial Physician and the Workers' Home Problems. C. W. Gatter.—p. 273.
ACTH (Corticotropin) in Industrial Medicine. J. A. Hubata.—p. 277.

SYMPOSIUM: MEDICAL SERVICES IN INDUSTRY

Viewpoint of the Profession. A. G. Kammer.—p. 282.
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The Industrial Physician—Past, Present, and Future. O. T. Mallery Jr. —p. 286.
Industrial Hygiene—Past, Present and Future. P. Drinker.—p. 288.
The Industrial Nurse—Past, Present and Future. M. L. Brown.—p. 291.
Report of Survey of Medical Services in Industry. R. C. Page.—p. 293.
*Traumatic Vasospastic Disease of Hand (Raynaud's Phenomenon). E. F Hoerner.—p. 297.

Traumatic Vasospastic Disease of Hand (Raynaud's Phenomenon).—During the past 10 years, disorders resulting from the use of vibratory tools have become more frequent due to the increased use in modern industry of such equipment. There are two types of vibratory tools. In the first class are those that employ the to-and-fro motion of a piston. Most compressed-air tools are of this type, such as rock drills, road rippers, mechanical picks, riveting, chiseling and chipping hammers, and pounding and lasting machines. The vibration is not so much a continuous oscillation as a series of short pulses with relatively long pauses between them. The second group of tools are those that rotate and are held in the hand, such as grinding and polishing equipment. Vibrations are not essential in the effective working of these tools, although, when they are used for grinding purposes, vibrations are inevitable. The disease produced by vibrating tools may be divided into the following clinical types: (1) Raynaud's phenomenon; (2) involvement of the bones, joints, and muscles of the upper extremities; and (3) a neuritic form. After a few months to several years of exposure to the vibrations, the patient notices attacks of blanching and numbness of the fingers. The pallor is much more pronounced than in Raynaud's disease, but it is not followed by the extreme asphyxia so characteristic of true Raynaud's disease. It is not symmetrical and is commoner in the left hand in right-handed persons, because the tool is held in the left hand. Some observers have advised that the worker should discontinue his exposure to vibratory tools on the first appearance of symptoms. Recovery may result when the use of vibratory tools is discontinued, but in others symptoms may persist. Careful selection of workers, changing of jobs, so that workers will not be exposed to vibratory tools continuously, reduction of exposure to vibration by insulation and shock absorbers, and proper holding of the vibratory tool are suggested as preventive measures.

Iowa State Medical Society Journal, Des Moines

42:201-244 (May) 1952

Recent Developments in Therapy for Essential Hypertension. W. M. Kirkendall.—p. 201.
Recent Advances in Otolaryngology. R. R. Updegraff.—p. 205.
Clinical Study of Bone Lesions in Malignant Lymphoma. J. H. Taylor. —p. 214.
Multiple Myeloma in General Practice. L. D. Amick.—p. 218.
Treatment of Pyogenic Skin Infections with Topical Neomycin. L. W. Kimberly.—p. 221.

42:245-286 (June) 1952

Care of Burns. M. L. Mason.—p. 248.
*Place of Version and Extraction in Present Day Obstetrics. W. C. Keettel and F. W. Crealock.—p. 251.
Sudden Death from "Pituitrin" Shock. J. E. Krettek and B. C. Russum. —p. 255.
Eye Manifestations of Head Injuries. H. H. Gurau.—p. 256.

Version and Extraction in Present Day Obstetrics.—With the increased safety of abdominal delivery, even when performed late in labor, the indications for internal version and extraction have gradually disappeared. Many practitioners, however, are still using this method in certain complications. In a table the authors list the incidence of podalic version by five year periods carried out at the University of Iowa Hospital in the years between 1926 and 1951. Before 1940 the incidence was 1%, but since then it has been reduced to 0.1%. The authors discuss observations made on the cases in which version and extraction was done, putting particular stress on the high fetal mortality. They feel that there are now only two indications for version and extraction; one is prolapse of the cord in a vertex presentation, with complete cervical dilatation where the presenting part is above the spines and the other indication is presentation of a second twin in a transverse position.

Journal of Experimental Medicine, New York

95:523-634 (June) 1952. **Partial Index**

Assay of Hypertensin from Arterial Blood of Normotensive and Hypertensive Human Beings. J. R. Kahn, L. T. Skeggs Jr., N. P. Shumway and P. E. Wisenbaugh.—p. 523.
Serum and Urinary Fibrinolytic Activity Related to Hemorrhagic Diathesis in Irradiated Dogs. J. Colgan, E. Gates and L. L. Miller. —p. 531.
Serial Transplantation of Rabbit Papillomas Caused by Shope Virus. R. Stanfield.—p. 543.
Experimental Globulin Glomerulonephritis in Rabbits. Morphological and Functional Changes. D. Waugh and R. H. More.—p. 559.
Studies on Inhibition of Proteolytic Enzymes by Serum. I. Mechanism of Inhibition of Trypsin, Plasmin, and Chymotrypsin by Serum Using Fibrin Tagged with I^{131} as Substrate. N. R. Shulman.—p. 571.

Journal of Infectious Diseases, Chicago

90:205-304 (May-June) 1952

Role of Spleen and Dynamics of Hemolysin Production in Homologous Anamnesis. W. H. Taliaferro and L. G. Taliaferro.—p. 205.
Chronic, Progressive Infection of Sheep's Lungs. B. Sigurdsson, H. Grimsson and P. A. Palsson.—p. 233.
Immunization Against Salmonella Infection in Breeding Colony of Mice. F. G. Carnochan and C. N. W. Cumming.—p. 242.
Therapy of Experimental Brucellosis. E. H. Kelly and A. N. Gorelick. —p. 249.
Embryonated Egg as Culture Medium for Animal Phase of Coccidioides Immitis. V. D. Newcomer, E. T. Wright and E. E. Tamblyn.—p. 258.
Superinfection in Experimental Brucellosis of Guinea Pigs. A. D. Pollack, E. H. Kelly, A. N. Gorelick and others.—p. 267.
Interference of Aureomycin with Activity of Penicillin in Vivo. P. Bartell. —p. 273.
Vaccination as Provoking Factor in Poliomyelitis: Experimental Approach. J. L. Melnick and N. Ledinko.—p. 279.
Acquired Resistance in Candida Albicans to Antibiotic Produced by Spore-forming Bacillus. L. E. Casida Jr. and E. McCoy.—p. 283.
Changing Picture of Encephalitis in Yakima Valley, Washington. W. C. Reeves, W. McD. Hammon, A. S. Lazarus and others.—p. 291.

Journal of Nutrition, Philadelphia

47:1-158 (May) 1952

Effects of Diet, Partial Hepatectomy and Growth-Promoting Factors on Composition of Rat Liver. M. E. Dumm, E. P. Ralli, H. Gershberg and B. Laken.—p. 11.
Protective Effect of Dietary Fat on Immature Rats Fed Thyroid. S. M. Greenberg.—p. 31.
Hepatic Necrosis Induced by Dietary Means: VI. Effect of Varying Level and Nature of Protein and Level of Fat on Development of Liver Necrosis. J. R. McLean and J. M. R. Beveridge.—p. 41.
Relationships Among Dietary Sterols, Plasma and Liver Cholesterol Levels, and Atherosclerosis in Chicks. D. W. Peterson, C. W. Nichols Jr. and E. A. Shneour.—p. 57.
*Cobalt Metabolism of Young College Women on Self-Selected Diets. M. J. Harp and F. I. Scoular.—p. 67.
Effect of Vitamin B_{12} and Amino Acid Imbalances on Growth and Levels of Certain Blood Constituents in Chick. Peng-Tung Hsu and G. F. Combs.—p. 73.
Comparative Biological Activity of Leucovorin and Pteroylglutamic Acid. H. P. Broquist, J. A. Brockman Jr., M. J. Fahrenbach and others. —p. 93.
Riboflavin in Human Serum. K. Suvarnakich, G. V. Mann and F. J. Stare.—p. 105.
Growth-Promoting Effect of Commercial Strained Meat and Fish Products Investigated with Infantile Rats. Ihsan El Rawi and E. Geiger.—p. 119.
Determination of Protein Requirement of Rat for Maximum Growth Under Conditions of Restricted Consumption of Food. H. H. Mitchell and J. R. Beadles.—p. 133.
*Improving Nutritive Value of Flour: V. Effect of Use of Defatted Wheat Germ. B. D. Westerman, F. Roach and M. Stone.—p. 147.

Defatted Wheat Germ for Improving Nutritive Value of Flour.—Several investigators have shown that enriching flour with thiamine, riboflavin, niacin, and iron is beneficial in promoting better nutrition. Wheat germ is one of the products removed when flour is milled, and this substance contains many vitamins and minerals as well as protein. After the removal of the oil, the wheat germ may be ground to a fine powder that mixes readily with the flour and has better keeping qualities than when the fat is present. On the basis of these facts the nutritive quality of defatted wheat germ used with enriched and non-enriched flour was studied in albino rats. Three methods of evaluation were used: the growth test, performance during pregnancy and lactation, and storage of the vitamins in the liver. The data obtained indicate that the addition of defatted wheat germ to the flour produced an increase in growth rate and better reproduction and lactation performance, as well as an increased storage of some vitamins, particularly pantothenic acid, in the liver.

Laryngoscope, St. Louis

62:449-546 (May) 1952. **Partial Index**

Recent Advances in Surgical Treatment of Facial Paralysis and Bell's Palsy. J. A. Sullivan.—p. 449.
Correlation of Predicted with Actual Result of Fenestration in 164 Consecutive Cases. G. E. Shambaugh Jr.—p. 461.
*Carcinoma of Larynx: Report of 194 Cases with 149 Laryngectomies. J. W. McCall and W. R. Fisher.—p. 475.
Afferent Representation of Larynx in Cerebellum. R. L. Lam and J. H. Ogura.—p. 486.
Fibrous Dysplasia. H. McCart.—p. 496.

Laryngectomy for Carcinoma of Larynx.—McCall and Fisher review the results obtained in 194 patients with cancer of the larynx observed from 1936 through 1950. Of this group, 27 had irradiation alone or refused treatment altogether. The Arbuckle procedure was done in nine patients. Fourteen laryngofissures were done, five of which were followed by laryngectomy. There were 149 laryngectomies and 18 radical neck dissections either at the time of or following laryngectomy. All but eight of the patients were men. Hoarseness was the predominant symptom, occurring as the only symptom in 57% of all cases and with other symptoms in 29%. Pain was the next commonest symptom, occurring in 19%; dysphagia occurred in 15%. The occurrence of hoarseness in a patient should be investigated. The fact that 5 of 14 patients treated by laryngofissure alone later required laryngectomy indicates that they were not selected with sufficient care. Eight of the nine patients who underwent the Arbuckle procedure had far advanced lesions and so it is not surprising that five died in less than six months. Eight of the 149 patients who were treated by laryngectomy died during the initial hospitalization. Of the 86 patients who were subjected to laryngectomy before 1946, 50 had extrinsic and 36 had intrinsic carcinoma. Half of those with intrinsic carcinoma, and only one-fifth of those with extrinsic growths survived more than five years following laryngectomy without evidence of disease. The overall five year survival rate for laryngectomized patients was 52%.

Memphis Medical Journal

27:79-91 (June) 1952

SYMPOSIUM ON OBESITY

Obesity and Heart Disease. P. Bleecker.—p. 80.
Obesity and Metabolic Disease. J. M. Hawkes.—p. 81.
*Problem of Weight Gain During Pregnancy. H. B. Turner.—p. 83.
Obesity as a Surgical Problem. C. E. Gillespie.—p. 83.
Discussion of Obesity. J. M. Bethea.—p. 85.

Weight Gain During Pregnancy.—Turner discusses normal gestational weight gain, excessive weight gain, and finally preexisting obesity and pregnancy. The average weight gain during normal pregnancy is about 22 lb. (10 kg.). This increase in weight is accounted for by the gestational products, the hyperplasia and hypertrophy of associated reproductive organs, and by water and protein storage. Almost one-half of the total weight gain is lost at the time of delivery. The remaining 10 to 12 lb. (5.4 kg.) is gradually lost. Excessive weight gain must be avoided, because it predisposes to eclampsia. Toxemia does not develop in women who during the critical period between the 20th and 30th weeks do not gain more than 8 lb (3.6 kg.). Apparently the rate of gain in weight is as important as the total gain. During the first trimester most women gain little or no weight and, because of nausea and vomiting, may sustain a weight loss during this period. It is during the latter six months of gestation that weight gain must be watched. Preexisting obesity makes prenatal management more difficult. The obese woman is predisposed to toxemia in the prenatal period, to dystocia, and to increased difficulty in delivery, and frequently, to residual hypertension in the puerperium and beyond.

Michigan State Medical Society Journal, Lansing

51:641-792 (June) 1952

Principles of Good Clinical Anesthesia. E. M. Papper.—p. 689.
Then and Now. N. R. Moore.—p. 693.
Vertigo: Diagnosis and Treatment. J. L. Dill.—p. 699.
Headaches: Etiology and Treatment. R. N. DeJong.—p. 701.
Chronic Intestinal Disease: Diagnosis and Treatment. T. T. Mackie. —p. 708.
Acute Abdominal Conditions. C. R. Doyle.—p. 715.
*Diabetic Coma: Prevention and Treatment. A. Marble.—p. 717.
Treatment of Alcoholism in an Out-Patient Clinic. F. A. Cellar and A. H. Grant.—p. 722.
Doctors' Fees and the Wage Earner's Dollar. N. E. Clarke.—p. 724.
Poliomyelitis and Injections. M. S. Cioffari.—p. 727.

Diabetic Coma: Prevention and Treatment.—The patient with diabetic coma should be hospitalized, since successful treatment depends on attention to details and close supervision by physicians and nurses. The urine should be tested for sugar and diacetic acid. Blood should be drawn for the determination of sugar, carbon dioxide content, nonprotein nitrogen, and other constituents. Diabetic coma is primarily a state of acute deficiency of insulin. Large amounts of insulin must be given early, that is, within the first two or three hours of treatment. In full-blown coma, several hundreds of units of insulin may be necessary. The initial dose given on admission may well be 100 units subcutaneously, with an additional 100 units intravenously. At one hour after admission, when the results of the blood sugar and carbon dioxide determinations are available, additional insulin may be given as follows: If the initial blood sugar is 300 to 600 mg. per 100 cc., 50 to 200 additional units; 600 to 1,000 mg. per 100 cc., 200 to 300 additional units; and over 1,000 mg. per 100 cc., 300 to 400 additional units. The second important factor is counteracting the dehydration with fluid and replacement of lost electrolytes. Since the stomach is often dilated, gastric lavage may be advisable, thereby relieving distention and paving the way for early institution of oral feedings. The patient should be kept warm by means of blankets rather than by hot water bottles or electric pads. No patient should die in or from diabetic coma unless there is an acute fatal complication.

New England Journal of Medicine, Boston

246:839-882 (May 29) 1952

Changing Pattern of Neurologic Medicine. D. E. Denny-Brown.—p. 839.
*Treatment of Thoracic Aortic Aneurysms by "Pack" Method of Intrasaccular Wiring. R. R. Linton and I. B. Hardy Jr.—p. 847.
Myasthenia Gravis: Report of Case with Exophthalmos, Without Hyperthyroidism, Relieved by Neostigmine. H. A. Hatch.—p. 856.
Asthma in Children: Follow-Up Study of 688 Patients After Interval of 20 Years. F. M. Rackemann and M. C. Edwards.—p. 858.
Routine Guaiac Stool Test. C. L. Holt.—p. 864.
Dr. Archagathos: Refugee Physician and Roman Consul. R. W. Buck.—p. 866.

Intrasaccular Wiring for Aortic Aneurysms.—Most thoracic aortic aneurysms are syphilitic in origin. Their incidence has been declining, undoubtedly as the result of control and more adequate treatment of syphilis. From 1942 to 1951 17 patients with syphilitic aneurysms and 1 with an arteriosclerotic aneurysm were treated at the Massachusetts General Hospital. This paper describes the results of a new "pack" method of intrasaccular wiring, which has been developed for the treatment of abdominal aortic aneurysms. Fusiform aneurysms may be treated by this method as well as the saccular type, despite statements to the contrary in the literature. Six patients had two aneurysms and the remainder had one. All but one of the 18 patients were men, and all but one of the aneurysms were fusiform in type. In earlier attempts at wiring, only 10 to 20 ft. of wire were inserted, and the authors feel that this largely explains the failures. In the majority of cases here described from 100 to 500 ft. of stainless steel wire were inserted. The wiring is best accomplished by direct exposure of the aneurysm through an open thoracotomy incision. Though not the ideal treatment, the "pack" method of wiring aneurysms has resulted in the relief of symptoms in the majority of the patients and in prolongation of life in a gratifying number.

246:883-918 (June 5) 1952

Antibiotic Therapy of Tuberculous Meningitis. L. Ravreby, G. H. Caron and V. A. Georgantas.—p. 883.
*Breast-Cancer Prognosis and Ovarian Cortical Stromal Hyperplasia. R. G. McManus and S. C. Sommers.—p. 890.
Periodic Neutropenia Treated by Adrenocorticotrophic Hormone and Splenectomy. R. W. Monto, H. C. Shafer, M. J. Brennan and J. W. Rebuck.—p. 893.
Acquired Fistula Between Esophagus and Respiratory Tract: Report of Case, Review of Literature and Discussion of Pathogenesis. R. B. Mellins.—p. 896.
Cystitis Emphysematosa: Case Report with Clinical Diagnosis and Review of Literature. W. A. Milner, W. B. Garlick and C. Mamonas.—p. 902.
Protection of Cardiac Glycosides from Action of Light by Actinic Desensitizer (Red Dye). T. M. Feinblatt and E. A. Ferguson Jr.—p. 905.

Prognosis of Breast Cancer and Cortical Stromal Hyperplasia of Ovaries.—The relationship between hyperplasia of the stroma of the ovarian cortex and cancer in women was first suggested by Smith in 1941. Recently Sommers and Teloh showed an association between this ovarian hyperplasia and cancer of the breast. In cases of stromal hyperplasia the ovaries appear grossly to be more nodular and bosselated than normal. Microscopically, there is an increased amount of cortical stromal whorling and fascicle formation. The nuclei are longer and broader than usual, collagen is scant and the reticular fibrils are relatively prominent. The authors became interested in the possible prognostic significance of these findings when two patients with breast cancer who were surgically castrated had no ovarian cortical stromal hyperplasia and died within one month. Histological sections of all ovaries removed for castration in breast cancer cases were then reviewed, the reviewers having no knowledge of the patients' clinical courses. Three of 31 cases were eliminated because the ovaries were largely replaced by tumor. The ovaries of 20 of the remaining patients were hyperplastic and the ovaries of 8 were atrophic. The survival time from onset of cancer to death differed in the two groups. The average survival time in the group with hyperplasia was 41 months and in those with atrophied ovaries it was 23 months. Thus the total duration of the disease in the women with ovarian cortical stromal hyperplasia was almost twice that of the patients who showed none. Women whose ovaries did not show cortical stromal hyperplasia survived longer following castration. The therapeutic effect of castration for carcinoma of the breast in women appears to be poor in the absence of cortical stromal hyperplasia of the ovaries.

New York State Journal of Medicine, New York

52:1271-1356 (May 15) 1952

Comparison of Usefulness of Dock Electromagnetic Ballistocardiograph and Exercise Tolerance Test in Detection of Coronary Insufficiency. S. H. Rinzler, H. Bakst and S. Rosenfeld.—p. 1277.
Cyclohexylmethylthiouracil in Treatment of Hyperthyroidism. G. J. Friedman, H. R. Marcus and J. J. Vorzimer.—p. 1281.
Packed Human Erythrocyte-Plasma Esterase Units for Transfusion Purposes; Preliminary Report. R. D. Barnard.—p. 1283.
Vaginal Discharge as Aid to Gynecologic Diagnosis. E. E. Lazarus.—p. 1287.
Use of Vitamin E in Treatment of Menopause. H. A. Gozan.—p. 1289.
Technic of Excision and Primary Closure of Pilonidal Sinus. E. O. Finestone.—p. 1291.
Bicuspid Aortic Valves and Bacterial Endocarditis. S. A. Mazar and N. Brown.—p. 1295.
Technic of Arthrodesis of Knee Utilizing Double-Tenon Block. A. A. Michele and F. J. Krueger.—p. 1299.
*Evaluation of Dicumarol Therapy in 300 Cases of Myocardial Infarction. I. H. Richter, R. F. Del Nunzio and S. L. Swiller.—p. 1301.
Pitfalls in Psychosomatic Diagnosis. A. N. Fleiss.—p. 1304
New Migraine Therapy. E. Foldes.—p. 1307.
Asthma as Disease of Dysreaction: New Therapeutic Approach. M. I. Salomon.—p. 1310.
Rheumatoid (?) Plantar Perifascitis and Its Response to Cortisone Therapy. O. C. Kestler.—p. 1313.
Cortisone Treatment in Essential Dysmenorrhea: Preliminary Report. F. Schuck.—p. 1316.

Bishydroxycoumarin in Myocardial Infarction.—A series of 300 patients with myocardial infarction were divided into two groups. Half of them received the customary treatment without anticoagulants; the remaining 150 received anticoagulant therapy in the form of bishydroxycoumarin (dicumarol®). The customary treatment includes the use of sedatives, narcotics, oxygen, papaverine, bed rest, and routine cardiac care. Both series of cases were unselected except for exclusion of patients who died within 72 hours and patients who were not hospitalized long enough for the results to be evaluated. In the series treated with bishydroxycoumarin the mortality was 11.3%, and in the control group the mortality was 33.3%. In the treated series the over-all incidence of thromboembolic complications was 10%, but was only 1.3% after effective therapeutic levels had been reached. In the control group the incidence of thromboembolism was 20%. In the treated group there were no deaths from thromboembolic complications, once the effective therapeutic level had been reached. When the cases were analyzed from the standpoint of previous attacks of myocardial infarction, it was apparent that the use of bishydroxycoumarin was invariably associated with the more favorable results. Thus results in this series support the view that bishydroxycoumarin is suitable adjunctive treatment in acute myocardial infarction.

Northwest Medicine, Seattle

51:373-464 (May) 1952

Advantages of Billroth I Resection with Report of Cases. R. D. Simonton.—p. 395.
Carpal Injuries. D. Ward.—p. 398.
Cholangiography as Aid to Biliary Surgery. J. L. Vadheim and F. J. Rigos.—p. 400.
*Paradoxical Cerebral Excision in Hemispastics: Preliminary Report. H. J. MacKay.—p. 403.

Hemispherectomy in Hemispastics.—MacKay says that his associate Rankin urged removal of all the damaged brain in a hemispastic child with cerebral palsy who was incapacitated by psychomotor seizures. At operation not only the left temporal lobe but the frontal, parietal, and occipital lobes were found to be atrophic. Since the left hemisphere was a useless, nonfunctioning tissue mass, it was totally removed. This patient regained consciousness promptly, demonstrated improvement of his spasticity, had no hemianopsia, and was not aphasic. He has not had a seizure of any kind since operation. Agreeing with Rankin, MacKay concludes that the damaged brain was functioning in an adverse way only. Its abnormal activity served to augment the patient's disability and produce seizures. Conversely, the good

hemisphere compensated for and assumed the functions of the damaged hemisphere. Amazed by the results obtained with cerebral excision in this patient, the authors performed the same operation on three other hemispastic patients, with the same gratifying results in each case. The authors comment on the fact that all four patients had left-sided brain lesions and that all hemispastic patients in their files had spasticity on the right side, presupposing left-sided brain involvement. This suggests that only those who have damage to the dominant hemisphere fail to show development consistent with a comparatively normal existence. MacKay suggests that in the past, the surgical treatment of cerebral palsy may not have been drastic enough.

Ohio State Medical Journal, Columbus

48:489-584 (June) 1952

*New Hope for Far Advanced Schizophrenia: Intensive Regressive Electroconvulsive Therapy in Treatment of Severely Regressed Schizophrenics. E. S. Garrett and C. W. Mockbee.—p. 505.
Tuberculosis and the New Drugs. R. H. Browning.—p. 510.
Hemorrhage in Pulmonary Tuberculosis; Treatment with Intravenous Procaine. O. Neufeld and F. R. Canelli.—p. 512.
Experience with Liver Biopsies in a Private Hospital. M. L. Meitus. —p. 515.
Proper Use of Sedatives. D. M. Palmer.—p. 518.
Hyperparathyroidism: Report of Four Cases Prior to Development of Bone Changes. S. R. Salzman.—p. 521.
Historical Notes on Use of Drugs to Accelerate Labor. J. E. Morgan. —p. 525.

Intensive Regressive Electroconvulsive Therapy in Schizophrenia.—Thirty severely regressed World War II veterans with chronic schizophrenia were chosen to undergo intensive regressive electroshock therapy in the hope that they might be brought into better contact with reality. Three grand mal type convulsions were induced daily, five days a week, until the patient reacted like a 3 or 4 year old child. The number of treatments required to reach this stage varied from 60 to 72. Increased respiratory difficulty was noted in all cases as treatment progressed, and near the end of each series oxygen was administered routinely following the grand mal reaction. A progressive "organic" syndrome was also recognized, and there were three cases of fracture. Encephalographic studies showed profound changes during and after treatment; all changes were transient in nature and no permanent ill effects were noted as a result of the treatment. An intensive program, consisting of intensive occupational and corrective therapy assignments, accompanied by psychotherapy, was carried on for a six month period during and after the electroconvulsive treatment. All the patients, with the possible exception of three, are improved to the extent that they require much less supervision, can care for their personal needs, and are no longer combative or suicidal. The authors believe that intensive regressive electroshock therapy fills a specific need and may be helpful to chronically ill schizophrenics.

Postgraduate Medicine, Minneapolis

11:471-576 (June) 1952

Physiologic Principles of Resuscitation and Oxygen Therapy. C. K. Drinker.—p. 471.
*Treatment of Brucellosis with Aureomycin or Terramycin Combined with Dihydrostreptomycin. W. E. Herrell and T. E. Barber.—p. 476.
Pneumoperitoneum in Treatment of Pulmonary Tuberculosis. J. A. Andosca.—p. 487.
Diagnostic Significance of "Lump in the Neck." H. Martin and C. Romieu.—p. 491.
Ruptured Cervical Intervertebral Disks. H. G. Schwartz.—p. 501.
Undiagnosing Coronary Thrombosis. C. M. Kurtz.—p. 507.
Early Diagnosis and Management of Gastric Lesions. G. C. Engel. —p. 513.
Frequency of Hepatitis in Doctors. S. Madsen.—p. 517.

Treatment of Brucellosis with Combinations of Antibiotics.—Of 60 patients with brucellosis, 53 were treated with aureomycin combined with dihydrostreptomycin and 7 were treated with terramycin combined with dihydrostreptomycin. These two combinations of antibiotics appeared to be equally effective. The authors had the impression, although not statistically proved, that patients may tolerate terramycin somewhat better than aureomycin. Of the 60 patients 43 had culturally proved brucellosis. Of these 43 patients 36 had the bacteremic form of the disease, which was caused by Brucella abortus, Brucella melitensis, or Brucella suis in 34, while the species causing the bacteremia in 2 was not definitely ascertained. Seven patients had culturally proved brucellosis with localizing lesions. The remaining 17 patients were acutely ill and had unmistakable evidence of brucellosis, although blood cultures were not positive. Two patients had bacteriological relapses and one had a symptomatic relapse. Re-treatment was necessary in two patients. This represents a clinical-bacteriological relapse rate of 5% and a recovery rate of 95%. The follow-up period in these patients usually lasted for from three months to more than two years. The plan of treatment advocated consists of daily administration of 3 gm. of either aureomycin hydrochloride or terramycin hydrochloride orally, and of 1 gm. of dihydrostreptomycin sulfate intramuscularly each morning and evening. In the acute bacteremic form of the disease and in the acute form without positive cultures this treatment should be continued for 12 to 14 days. In the presence of localizing forms of the disease, the same dose of terramycin or aureomycin should be administered orally for 28 days. The daily dose of dihydrostreptomycin in these cases should be reduced to 1 gm. daily, administered intramuscularly in doses of 0.5 gm. each morning and evening. The combined use of terramycin or aureomycin and dihydrostreptomycin has not been presented as a specific treatment of brucellosis, but the results to date justify the conclusion that this combined treatment is far superior to any other currently available method. Furthermore, the undesirable toxic reactions at times observed with other methods have not been encountered.

Southern Medical Journal, Birmingham, Ala.

45:477-580 (June) 1952. **Partial Index**

Chronic Perforating Carcinoma of Colon. C. A. Stevenson and A. W. Sommer.—p. 477.
Factors Influencing Prognosis of Cancer of Colon. R. R. White.—p. 481.
Benign Tumors of Ureter. W. V. Pierce and W. R. Miner.—p. 485.
Medical Uses of Cobalt. H. D. Kerman.—p. 495.
Aneurysm of Ascending Aorta. J. E. Miller.—p. 503.
Surgical Training for General Practitioner. R. T. Smith.—p. 511.
Coxsackie Viruses. Properties, Immunological Aspects and Role in Human Disease. S. E. Sulkin.—p. 516.
Respiratory Acidosis and Alkalosis. F. S. Hill.—p. 521.
Prolonged Vomiting as Cause of Potassium Deficiency. B. A. Shatz and F. J. Catanzaro.—p. 525.
*Attenuated Virus in Autogenous Blood Serum as Therapeutic Agent in Herpes Zoster. C. P. Bondurant.—p. 529.
Carcinoma of Ovary: Newer Aspects. W. F. Guerriero, J. W. Tabler and C. Bruce.—p. 533.
Treatment of Mass Burns. B. W. Haynes Jr.—p. 545.
Industrial Hygiene Problems as Seen by Workman Compensation Carrier. H. T. Herndon.—p. 551.
Cortisone in Acute Rheumatic Carditis. J. A. Boone and M. W. Beach. —p. 556.
Treatment of Acute Hematogenous Osteomyelitis in Children. B. E. Batson.—p. 562.
Pathology of Abnormal Uterine Bleeding. R. A. Street Jr.—p. 569.

Therapy of Herpes Zoster.—Bondurant uses attenuated or inactivated virus in autogenous blood serum in treatment of herpes zoster, pointing out that this is one of the oldest methods of combatting infectious diseases, and that the earliest work was done on diseases of viral etiology, in smallpox by Jenner and in rabies by Pasteur. Bondurant reasoned that the blood serum taken in the active phase of herpes zoster can be assumed to contain the virus. He withdraws 30 cc. of blood, allows it to coagulate under refrigeration, and after centrifugation obtains the serum. This serum is then heated in a hot water bath at 56 C for 30 minutes, and is cooled and injected intramuscularly. It is important to keep the water bath below the coagulation temperature, which is 60 C. The attenuated serum is given in daily doses of 5 cc. each, usually in a course of 6 to 10 doses. The author also used whole blood that had been prepared as for transfusion, but he feels that the use of serum is the better of the two methods. The treatment is less effective in mild cases, since apparently a certain severity is necessary to induce a fairly sharp virulent reaction. The clinical data on 10 cases treated with the autogenous blood serum are presented in a table, and the results obtained indicate that the attenuated virus in autogenous blood serum is valuable in the treatment of herpes zoster.

FOREIGN

Acta Medica Scandinavica, Stockholm

143:1-82 (No. 1) 1952. **Partial Index**

Skeletal Changes in Adults with Diabetes Mellitus. C. A. Hernberg. —p. 1.
Chronic Cor Pulmonale in Bronchial Asthma, Chronic Bronchitis, Bronchiectasis and Pulmonary Emphysema. S. Samuelsson.—p. 15.
*Antibacterial Drugs in Acute and Chronic Mucopurulent Bronchitis due to Hemophilus Influenzae. J. Mulder, W. R. O. Goslings, M. C. van der Plas and P. Lopes Cardozo.—p. 32.

Antibacterial Drugs in Acute and Chronic Mucopurulent Bronchitis.—Sulfonamide compounds, penicillin, streptomycin, chloramphenicol (chloromycetin®), aureomycin and terramycin, or a combination of penicillin and streptomycin were used in treatment of 125 adults with mucopurulent bronchitis. In most cases, including those of infectious asthmatic bronchitis, the bronchitis was associated with bronchiectasis. Bacteriological examination of the sputum of these patients yielded nonencapsulated Hemophilus influenzae. Observations were made of the in vitro sensitivity of the Hemophilus organism and the concentration of the various antibacterial drugs in the blood and sputum of the patients. By using large enough doses of the various drugs, it was possible to eliminate Hemophilus organisms from the sputum of most patients, and this effect was accompanied by disappearance or improvement in the clinical symptoms. It may be concluded therefore that in these patients H. influenzae must have been the etiological agent of the inflammation. Results of treatment with the antibacterial drugs were as follows: Sulfonamides were valuable in treatment of acute bronchial infections due to H. influenzae but not in treatment of chronic mucopurulent bronchitis associated with bronchiectasis. Penicillin was most effective when administered parenterally in chronic Hemophilus bronchitis. Administration of aerosol penicillin was technically difficult, and was effective only with large doses of 200,000 units five times daily. Doses of 4,000,000 units of penicillin daily were required by intramuscular route. In acute and chronic Hemophilus bronchitis good results were obtained with 4,000,000 units of penicillin and 2 gm. of streptomycin administered intramuscularly daily, penicillin being given for 5 to 10 days and streptomycin for 5 days. Chloramphenicol in doses of 2 gm. daily for about 14 days was effective; with shorter periods of treatment the number of relapses was high. Aureomycin and terramycin were effective in similar doses, but for financial reasons the number of patients treated was small. Of the 51 patients treated successfully with the methods other than administration of aerosol penicillin, 29 had relapses of Hemophilus bronchitis. Prolonged treatment with 200,000 units of aerosol penicillin daily in the outpatient department or at the patient's home appeared to be inadequate, since of 64 patients so treated 41 had relapses. Treatment with antibacterial drugs effective against the Hemophilus group according to the described schedules is especially recommended in cases of acute Hemophilus bronchiolitis (primary, or complicating measles, influenza, pertussis, and bronchiectasis) and for preoperative and postoperative management of pneumonectomy, lobectomy, or segmental lung resection in patients with bronchiectasis.

British Medical Journal, London

1:1093-1144 (May 24) 1952

Concepts of Rheumatic Disease. J. H. Kellgren.—p. 1093.
Megaloblastic Anaemia in Young Adults: Aetiological Importance of Occult Idiopathic Steatorrhoea. H. Conway.—p. 1098.
Risks of Needle Biopsy of Liver. R. Terry.—p. 1102.
Investigations into Cause of Microfilarial Periodicity. J. A. McFadzean. —p. 1106.
Effect of Hypochromasia on Specific Gravity and Sedimentation of Red Cells. K. B. Rogers.—p. 1109.
*Tattooing as Possible Means of Transmitting Viral Hepatitis. A. C. S. Hobson, D. E. Fraser and N. H. Newman.—p. 1111.
Polycythaemia and Myelosclerosis. F. G. Marson and M. J. Meynell. —p. 1113.
Tinea Capitis (M. Audouini) in a Residential School. A. L. Walby. —p. 1114.

Transmission of Viral Hepatitis by Tattooing.—The term "viral hepatitis" was proposed by Neefe and associates in 1946 to describe the forms of hepatitis caused by filterable infectious agents that have not yet been isolated and identified. Experiments on human volunteers have shown that at least two virus-like agents are involved in the etiology of viral hepatitis. These two agents have been called virus IH and virus SH. Virus IH is present in the feces and blood, and is related to infectious hepatitis (incubation period of 15 to 40 days), while virus SH is found only in the blood and is related to homologous serum hepatitis (incubation period of 50 to 150 days). Both viruses appear in the blood, and parenteral transmission of such blood may cause hepatitis following an incubation period typical of either virus. That tattooing should be regarded as an important means of dissemination of viral hepatitis was suggested by the fact that in a hospital for service personnel in Hong Kong the number of tattooed patients was higher in the hepatitis wards than in other wards. Investigations on 143 patients with viral hepatitis in this hospital disclosed that 56, or 39.1%, had been tattooed 51 to 150 days beforehand, as against 16, or 10.5%, of 152 controls in the same hospital. The technique of tattooing facilitates transmission of the hepatitis virus, since the needle is not sterilized before use in successsive persons. Furthermore the bottles of dye may also become infectious.

Canadian Journal of Medical Sciences, Ottawa

30:157-294 (June) 1952. **Partial Index**

"In Vivo" and "In Vitro" Effect of Ascorbic Acid and ACTH on Rat Adrenal Cortex. A. DesMarais and J. Leblanc.—p. 157.
Concentration and Accumulation of Lipids in Tumor Component of Tumor-Host Organism, Walker Carcinoma 256 in Albino Rats. E. M. Boyd and H. D. McEwen.—p. 163.
Wallerian Degeneration in Rat: Chemical Study. W. A. Mannell.—p. 173.
Nucleodepolymerase Activity in Regenerating Rat Liver. R. Daoust, G. de Lamirande and A. Cantero.—p. 180.
Radio-Frequency Rewarming in Resuscitation from Severe Hypothermia. W. G. Bigelow, J. A. Hopps and J. C. Callaghan.—p. 185.
Preparation of Stable Noninfective Soluble Influenza A Antigen: II. Use of Various Reagents for Neutralization of Formaldehyde-Treated Antigens. J. R. Polley.—p. 194.
Absorption and Fluorescent Properties of α-Estradiol Sulphuric Acid Complex. J. H. Linford.—p. 199.
Cultivation of Poliomyelitis Virus in Tissue Culture: I. Growth of Lansing Strain in Human Embryonic Tissues. J. C. Thicke, D. Duncan, W. Wood and others.—p. 231.
Tularemia Among Beaver and Muskrat in Ontario. N. A. Labzoffsky and J. A. F. Sprent.—p. 250.
Study of Liver Function in Dogs. A. G. Gornall and C. J. Bardawill. —p. 256.
*Influence of Dietary Protein on Liver Injury Due to Carbon Tetrachloride in Dogs. C. J. Bardawill and A. G. Gornall.—p. 272.
Method for Quantitative Measurement of Agglutinin Nitrogen in Antisera to Hemophilus Pertussis, Phase I. C. F. C. MacPherson, P. H. Maurer, H. E. Alexander and W. Redman.—p. 284.

Influence of Dietary Protein on Liver Injury.—Six adult dogs that had been previously exposed to carbon tetrachloride and allowed a recovery period of seven months were kept at different times on isocaloric, low protein, and moderately high protein diets. During each of these periods 16 consecutive doses of carbon tetrachloride were administered. Liver function was tested fortnightly by means of the sulfobromophthalein (bromsulphalein®) excretion test, serum alkaline phosphatase determinations, and serum protein fractionation. Biopsy specimens were also examined. There was considerable variation from one dog to the next. Analysis of the data indicated that the acute phase of liver injury during carbon tetrachloride administration was accompanied by less derangement of function when the dogs were on a low protein diet. In the recovery phase the higher protein intake resulted in a somewhat more rapid restoration of function. It is suggested that some restriction of protein is probably desirable during the acute phase of a destructive liver lesion. Once recovery and regeneration set in, however, generous amounts of protein in the diet will tend to hasten the repair process.

Gazzetta Medica Italiana, Milan

111:103-126 (April) 1952. **Partial Index**

p-Aminobenzoic Acid as a Presumed Antiallergic Substance. A. Pani. —p. 103.
Aluminum Therapy: Clinical Report. A. Paolini and G. Raineri.—p. 107.
*Diethylstilbestrol in Mumps Orchitis. G. Butti.—p. 111.

Diethylstilbestrol in Mumps Orchitis.—The fact that orchitis secondary to mumps occurs almost exclusively in adult patients suggests that the virus seldom attacks inactive testes. For this reason diethylstibestrol was used as a therapeutic and prophylac-

tic drug to decrease the activity of the testes and cause them to revert to the prepubertal type of gland. Thus, the probability of their becoming infected by the virus is decreased or, when the infection is already present, the severity and length of its course are reduced. The indicated dosage is 1 to 2 mg. daily for prophylaxis and 4 to 6 mg. for therapy for the entire febrile course and sometimes for a shorter period. The author gave 6 mg. of diethylstilbestrol daily for four to six days to six young men with mumps orchitis. General and local symptoms disappeared sometimes after 24 to 48 hours. Complete recovery was obtained within 8 to 10 days, and there were no side-effects. A dose of 2 mg. of diethylstilbestrol was also given daily for 6 to 10 days to seven other patients with acute mumps. Orchitis did not occur in any of these patients, whereas it developed at the same time in other patients from the same region who had mumps but who had not received diethylstilbestrol.

Glasgow Medical Journal

33:143-200 (May) 1952. **Partial Index**

Some Circumstances Affecting Survival of Premature Children. A. E. Ferguson, A. C. Brown and T. Ferguson.—p. 143.
*Acute Appendicitis in Young Child. W. M. Dennison and D. A. Macpherson.—p. 175.

Acute Appendicitis in Young Child.—In children less than 3 years old the diagnosis of appendicitis is frequently overlooked in the early stages, and in the present series the appendix had ruptured in over 90% of cases before the patient was hospitalized. This communication describes some of the problems encountered in dealing with 82 cases of acute appendicitis in children under 3 years of age admitted to one surgical unit at the Royal Hospital for Sick Children, Glasgow, during the five year period 1946 to 1950. Until 1946 approximately 10 children less than 3 years old with acute appendicitis were admitted to this surgical unit. During the past two years the incidence of the disease in this age group has increased until in 1950 there were 27 cases. Six of the children had simple acute appendicitis, 15 had appendicitis with local peritonitis, 36 had an abscess containing a gangrenous appendix walled-off from the peritoneal cavity, and 25 had appendicitis with diffuse peritonitis. Abdominal pain, vomiting, elevation of temperature, and either constipation or diarrhea are the commonest symptoms; 20 of these children had been given purgatives. Leukocytosis is usually present, but since it is also found in other conditions, other possible causes must be ruled out. Examination of the throat and chest must never be omitted, and infections of the urinary tract, infectious hepatitis, deep iliac adenitis, tuberculous mesenteric adenitis, inflammation of Meckel's diverticulum, torsion of the omentum and other conditions should be considered in the differentiation. In 77 cases it was possible to remove the appendix at the initial operation. In three instances the surgeon considered it wiser to evacuate the pus only and to remove the appendix at a later date. Expectant treatment was adopted in two cases with appendiceal abscess. The appendix was removed three months later. The five deaths occurred in patients with diffuse peritonitis with overwhelming toxemia. The authors stress that the diagnosis is made late in too many cases, and the chief reason for delay in diagnosis is failure to suspect appendicitis in this age group.

Indian Medical Gazette, Calcutta

87:37-84 (Feb.) 1952

Action of Metals on Bacteria. C. O Karunakaran and K. V. Pillai.—p. 37.
Acute Arterial Occlusion with Case Report. K. N. Udupa.—p. 40.
Hypnosis in Intermittent Claudication: Report of Case. J. S. Nallapa.—p. 43.
*First Results of Mass Vaccination with B.C.G. in India. K. S. Ranganathan.—p. 62.

First Results of Mass BCG Vaccination in India.—India was the first country in Southeast Asia to launch a mass BCG vaccination campaign against tuberculosis with the help of the World Health Organization joint enterprise. The great distance separating India from the BCG vaccine laboratories in Europe, the difficulties of transporting the vaccine under cold storage conditions, and the large quantities required made it necessary to establish a center for producing the vaccine in India itself. The production of vaccine for the campaign throughout India and some nearby countries has been centralized in a single laboratory, thus ensuring uniform potency. Solutions of purified tuberculin in buffered saline are also supplied to all the vaccination centers in India by the BCG vaccine laboratory. Various methods of tuberculin testing were tried at the outset of the campaign; in June, 1950, a single screening test with five tuberculin units, as proposed by the World Health Organization's expert committee on tuberculosis, was adopted. The vaccine now used contains 0.5 mg. of BCG mass per milliliter, and is transported in refrigerated containers. The BCG is given by intracutaneous injection only. The efficacy of BCG vaccination in controlling morbidity and mortality from tuberculosis in India cannot be assessed for many years, but certain points of interest have already been noted. The over-all conversion rate of 84.7% shown by a control group of 14,508 persons who were vaccinated and retested with tuberculin from 6 to 10 weeks later compares favorably with the figures obtained by the joint enterprise in Greece, Austria, Jugoslavia, and Czechoslovakia. A more uniform technique of testing and vaccination, which is not easy to secure under the widely varying climatic and physical conditions in India and with the large numbers of doctors and nurses engaged in the campaign, will doubtless result in a greater percentage of conversions. The complete absence of serious complications among the 1,265,135 individuals so far vaccinated shows that BCG vaccine is harmless to the Indian population.

Irish Journal of Medical Science, Dublin

317:193-240 (May) 1952

*Pneumoconiosis in Irish Colliery Workers. J. Deeny, N. F. Walsh and M. M. Conran.—p. 193.
Prolonged Labour—Three Years' Survey. M. Solomons.—p. 207.
Denmark's Anti-Tuberculosis Campaign. K. Winge.—p. 218.
Consideration of Some of the Problems Presented by Epilepsy. R. Thompson.—p. 227.
Temporal Arteritis: A Case. R. Wilson.—p. 235.

Pneumoconiosis in Coal Miners.—Screening by 70 mm. miniature roentgenograms was carried out on 1,133 of 1,324 workers in Irish coal mines. Those in whom the microfilms showed abnormalities were subjected to more detailed examinations. Simple pneumoconiosis was found in 60, and complicated pneumoconiosis in 18 workers. Three stages of pneumoconiosis were observed: The first stage was characterized by dry bronchitis. In the second stage there was a more pronounced bronchitis, thought to be related to the nodular stage characterized by small aggregates of lymphoid tissue in the lungs and fine fibrosis. The third and severer stage, was believed to be indicative of gross fibrosis complicated and possibly produced by a superimposed, not necessarily tuberculous, infection. None of these stages was a distinct clinical entity, as the disease gradually progresses from one stage to another. A slight degree of orthopnea and perhaps a few dry ronchi were noticed, but few complaints were made during the first stage. In the second stage, orthopnea was more pronounced, and the symptoms were those of chronic bronchitis. In the third stage most of the men were not fit for work, being dyspneic on normal quiet walking. The authors feel that coal miners should undergo roentgenologic screening every year. Although pneumoconiosis was not as frequent in Irish miners as among coal miners in other regions, it nevertheless represents a real hazard. Hardness of the coal and the presence of quartz or silica in the rock formations of the mines largely determine the incidence of pneumoconiosis, as does also the length of time spent in mining, but individuals differ in susceptibility. Men from healthy families were less likely to develop the condition than those from sickly families. Men who, in addition to being miners, also worked on their small farms had a low incidence of pneumoconiosis.

Journal of Bone and Joint Surgery, London

34B:1-166 (Feb.) 1952

Spontaneous Fractures of Both First Ribs. S. A. Jenkins.—p. 9.
*Interinnomino-Abdominal Operation: Observations on Series of 50 Cases. G. Gordon-Taylor, P. Wiles, D. P. Patey and others.—p. 14.
Reposition with Arthroplasty for Congenital Dislocation of Hip in Adults. R. M. D'Aubigné.—p. 22.
Sprung Back. P. H. Newman.—p. 30.
Localized Osteochondritis (Scheuermann's Disease). R. H. V. Hafner. —p. 38.
Traumatic Prepatellar Neuralgia. C. G. Gordon.—p. 41.
Congenital Fusion of Lunate and Triquetral Bones in the South African Bantu. A. B. deVilliers Minnaar.—p. 45.
Transfer of Tibialis Anterior Tendon for Relapsed Club-Foot. J. E. Critchley and R. G. Taylor.—p. 49.
Chondro-Osteo-Dystrophy. J. R. Brailsford.—p. 53.
*Traumatic Chylothorax: Case After Dislocation of Thoracic Spine. P. R. Wright and A. M. N. Gardner.—p. 64.
Fracture of Pelvis Complicated by Ischaemia of Lower Limb: Report of Case. J. N. Wilson.—p. 68.
Combined Injury of Popliteal and Posterior Tibial Arteries: Report of Case. N. W. Nisbet.—p. 70.
Dislocation of Shoulder Complicated by Rupture of Axillary Vessels: Report of Case. J. R. Kirker.—p. 72.
Fibular Transplant for Osteoclastoma of Radius. T. L. Lawson.—p. 74.
Joint Changes in Neurofibromatosis: Report of Two Cases. A. C. Bingold.—p. 76.
Salmonella Dublin as Cause of Chronic Osteomyelitis: Report of Case. R. W. Lawrie.—p. 80.
Dysplasia Epiphysialis Multiplex in Three Sisters. W. Waugh.—p. 82.
Unusual Fracture-Dislocation of Spine: Report of Case. M. E. Winston. —p. 88.
Flake Fracture of Talus Progressing to Osteochondritis Dissecans. K. L. Marks.—p. 90.
Malignant Osteoclastoma: Report of Case. J. A. P. Cameron and A. T. H. Marsden.—p. 93.

Interinnomino-Abdominal Operation.—In the 50 cases reviewed in this paper interinnomino-abdominal operations were done by surgeons of the Middlesex Hospital between 1922 and 1950. Thirty-three patients were men and 17 were women. The ages ranged between 14 and 60, and eight were less than 20. Twenty-six patients had bone tumors, 23 had soft tissue tumors, and 1 had extensive persistent osteomyelitis. Amputation through the pelvic girdle was necessary in all cases because of the position of the lesion and because it offered the only reasonable hope of saving or prolonging life; in some cases the operation was done to relieve intolerable pain, or because the limb had become a useless encumbrance. In some cases local resection and radiotherapy had not been successful. Of 26 amputations for bone neoplasms, 18 were for tumors of the pelvic girdle and 8 for tumors of the upper end of the femur. In the femur osteogenic sarcoma was the commonest tumor and in the pelvic girdle chondrosarcoma. Of the soft tissue tumors 19 were spindle-cell sarcomas or fibrosarcomas, and most of these were distal to the inguinal ligament. The technique of the operation is described. There were 11 surgical deaths, mostly caused by shock and hemorrhage. Only one of the 11 amputations in patients over 50 was fatal. There has been a considerable reduction of mortality in the last decade (only 7 deaths in 39 cases compared with 4 in 11 cases before 1940). There were 5 fatal cases among the 17 in which amputation had to be combined with sacroiliac disarticulation. Twenty-two of the 50 patients are alive today, and 10 of them have survived more than five years. Since the lesions would have been fatal without the operation, it is justified despite its high mortality rate and inevitable mutilation. What the shorter survival figures fail to show is the relief from pain that the procedure usually affords as well. The contribution to the patients' well-being is considerable, even though death from pulmonary metastases may occur a few months later. It is to be regretted that in some cases reasonable prospect of cure has been denied the patient because amputation has been undertaken only after repeated and inadequate local excisions. In others there has sometimes been no real attempt at cure at all, and amputation has been passed over in favor of a palliative operation or of radiotherapy, reducing the chances of effective amputation.

Traumatic Chylothorax After Dislocation of Thoracic Spine.—In the case reported here a 27-year-old man had been crushed inside the cab of a truck. His lower limbs were paralyzed, and he had loss of sensation, which indicated complete interruption of the spinal cord in the midthoracic region. Manipulative reduction of the spinal dislocation was performed on the third day. His condition remained favorable for two days, but suddenly became worse; he became cyanotic, lost consciousness, and died. Necropsy revealed 1.5 liters of fluid in each pleural cavity; the fluid resembled thin coffee but was tinged with red. It contained some fat and protein; it was still opaque after it had been centrifuged, and the deposit consisted of red cells and many lymphocytes, with a few macrophages and endothelial cells. Thus the chylous nature of the fluid was certain, but unfortunately its source was not demonstrated, and it must be presumed that there had been severe injury to the thoracic duct at the site of the spinal dislocation. The authors point out that symptoms of chylothorax usually do not appear until three to four days after injury. It has been assumed that the chyle at first accumulates in the posterior mediastinum, and it is only after several days that the pleura on one or both sides gives way and allows a sudden leakage of fluid into the pleural cavity. Symptoms then appear suddenly and are at first referable only to the mechanical effects of the large pleural effusion. A second group of symptoms appears due to the loss of fat, protein, and fluid. In the case described here the pleura on both sides must have been torn at the time of injury, but chyle formation must have been greatly restricted at first. It is assumed that a sudden increase in flow took place immediately before death. This may have been due to the following sequence of events: (1) hemoconcentration, with increased osmotic pressure of the plasma proteins diminishing lymph formation; (2) ingestion of fluid and food, which increases lymph flow in the thoracic duct; (3) anoxia, which, by increasing the permeability of capillary endothelium, augments lymph formation; and (4) increase in venous pressure. A "vicious circle," initiated by an increased food and fluid intake, seems to provide a likely explanation of the delayed but sudden collapse in this case, and may well apply to other cases of traumatic chylothorax.

Lancet, London

1:1029-1076 (May 24) 1952

*Electro-Encephalogram in Doubtful Cases of Epilepsy. E. C. O. Jewesbury.—p. 1029.
Pancreatic Enzyme Activity in Duodenal Contents of Children with a Type of Kwashiorkor. M. D. Thompson, and H. C. Trowell.—p. 1031.
Chemotherapy for Staphylococcus Aureus in Burns. E. J. L. Lowbury, A. M. Hood and E. Topley.—p. 1036.
Ability of Normal Kidney to Conserve Potassium. P. Fourman.—p. 1042.
Effect of 3:5:3'-L-Triiodothyronine in Myxoedema. J. Gross, R. Pitt-Rivers and W. R. Trotter.—p. 1044.
Controlled Hypotension and Its Effect on Renal Function. B. Evans and G. E. H. Enderby.—p. 1045.
*Irradiation of Retinoblastoma (Glioma Retinae). H. B. Stallard.—p. 1046.

Electroencephalogram in Epilepsy.—Jewesbury believes that there is a fairly widespread tendency to overestimate the diagnostic value of the electroencephalogram in doubtful cases of epilepsy. He discusses nonspecific dysrhythmia and abnormalities of the electroencephalogram in epileptic and in normal people. He concludes that perhaps the most interesting achievement of the electroencephalogram in relation to epilepsy has been the light that it has thrown on the inherent tendency to epilepsy and allied disorders in people who have never had a fit. Instability of the electroencephalogram occurs oftener in young people, and the electroencephalograms of some apparently normal persons show delta waves on overbreathing if their blood suger level is rather low. The degree of disturbance of the electroencephalogram depends largely on the nature of the epileptic attack and the patient's age. The finding of normal rhythms or nonspecific dysrhythmia in the electroencephalogram is of little diagnostic value, and may confuse the issue in the case of a doubtful history of epilepsy. The likelihood of finding an electroencephalographic pattern diagnostic of idiopathic epilepsy in a patient whose fits start comparatively late in life is slight. Unfortunately, this is just the sort of case in which the electroencephalogram is especially in demand. In cases of head injury followed by alleged epilepsy the electroencephalogram cannot always provide a dogmatic answer about the nature of the attacks. When an epileptic seeks advice on marriage and parenthood, it is sometimes recommended that the proposed partner should also undergo electroencephalography. Both are reassured if this is normal, but, if a nonspe-

cific dysrhythmia is discovered in each, an element of uncertainty is introduced. The author feels that anything other than paroxysmal dysrhythmia should be discounted in such cases. Specific electroencephalographic changes and epileptic attacks can be induced in some apparently normal people by special "activating procedures." Perhaps those who are sensitive to hypoglycemia, "flicker," or leptazol (pentylenetetrazol) have a less stable cortical rhythm, and are therefore more liable to develop epilepsy or allied disorders than their fellows, but to regard such people clinically as potential epileptics is unjustifiable.

Irradiation of Retinoblastoma.—Stallard says that, although it has been stated that tumors arising in radioresistant tissue are invariably radiorefractory, this is not true of retinoblastoma (glioma retinae); although the retina, like other parts of the nervous system is resistant to irradiation, the undifferentiated atypical cells of retinoblastoma are radiosensitive. In answer to the question whether retinoblastoma should be treated by radium or by deep x-rays, the author cites his own observations in 29 unselected cases. In 16 cases he treated the tumors with 2 mC radon seeds from 1934 to 1948, and in 13 (14 eyes) with curved radium disks from 1948 to 1951. He also mentions observations by other investigators. He gained the impression that when a third or less of the retina is involved in a retinoblastoma, there is reasonable hope that the new growth may be destroyed by irradiation. With very few exceptions the results are bad when half or more of the retina is already destroyed. In such cases the retina is usually detached; if it is not, it will almost certainly become detached following irradiation. Later sequelae are severe intraocular hemorrhage, iridocyclitis, complicated glaucoma, and endophthalmitis. Irradiation often fails when the choroid is infiltrated. It seems advisable in such advanced cases to excise the eye with 10 mm. of the optic nerve and to irradiate the orbit postoperatively. In no case of the advanced type was irradiation of the eye worth while. The dose is still empirical. The neoplasm in some patients is more radiosensitive than in others, and the retinoblastoma seems more radiosensitive than the more highly differentiated neuroepithelioma. A dose of 2,500 to 3,000 r at the summit of the neoplasm and up to 6,000 to 8,000 r at its base is generally effective. The source of radiation should be as close as possible to the eye, and and the irradiation applied quickly in doses that are both effective and reasonably safe for the eye. Radium disks, made to fit the scleral curvature evenly, are better than radon seeds and other applicators used hitherto. Although deep x-ray treatment is successful in some cases in which less than a third of the retina is involved, it has the technical disadvantage of protracted treatment, with the difficulty of maintaining the child's head immobile during treatment, and it produces a higher incidence of serious complications than application of a radium disk or a radon seed.

Medicina, Buenos Aires

12:1-64 (Feb.) 1952. **Partial Index**

*Effect of Methylthiouracil and Propylthiouracil on the Number of Circulating Eosinophils and Eosinophil Precursors in Bone Marrow in Hyperthyroid and Normal Subjects. F. A. de la Balze, R. Celani Barry, F. C. Arrillaga and R. E. Mancini.—p. 1.

*Iodine Deficiency in Human Thyroid Gland. H. Perinetti, E. B. del Castillo, J. E. Itoiz and others.—p. 17.

Anatomical Study of Adrenals, Spleen and Testicles of Guinea Pigs During Reaction of Alarm and Phase of Resistance. O. C. Croxatta and J. Chiriboga.—p. 37.

Effect of Thiouracil on Circulating Eosinophils.—The effect of thiouracil derivatives on circulating eosinophils and the eosinophil precursors in the bone marrow was studied in 21 hyperthyroid and 9 euthyroid persons. Methylthiouracil was given to 22 patients and propylthiouracil to 6; 2 patients received both drugs alternately. Similar changes were noted in both the euthyroid and the hyperthyroid groups. The results showed that administration of these thiouracil derivatives sometimes causes disappearance of the circulating eosinophils and eosinophil precursors in the bone marrow. The time and dosage required to bring about these changes vary; in some of the patients the circulating eosinophils declined in number but did not completely disappear. The reversibility of the changes was indicated by the reappearance of eosinophils in the peripheral circulation and a return of the sternal bone marrow to normal after reduction or discontinuance of the medication. Five hyperthyroid patients showed an increase in the number of circulating eosinophils, which coincided with improvement in the hyperthyroid condition. This was perhaps due to the fact that thiouracil derivatives probably act on hyperthyroid patients in two different ways: (1) directly, on the bone marrow, and (2) indirectly, through modifications of the adrenal cortex, which appear as a result of changes in thyroid function.

Iodine Deficiency in Human Thyroid.—A study of endemic goiter is being conducted in Mendoza in Argentina under the auspices of the goiter division and institute of the Province of Mendoza and the National University of Cuyo respectively and the thyroid clinic of the Massachusetts General Hospital. Radioiodine (I^{131}) and exact methods of determining stable iodine (I^{127}) were used in investigating thyroid dynamics in 122 clinically euthyroid patients under 35 years of age, most of whom had diffusely enlarged thyroids. The up-take of radioactive iodine in the thyroid was measured with a Geiger-Mueller counter. Although there were wide variations, in a large number of the patients more than 60% of the dose given was accumulated at the end of 48 hours. The amount of I^{127} in the diet was measured by the quantity excreted daily in the urine; many of the patients studied eliminated less than 10 μg. of iodine daily. A low excretion rate of I^{127} was accompanied by a high up-take of I^{131} in most cases; only once was a high up-take accompanied by a comparatively high excretion. The iodine-deficient thyroid not only accumulates iodine rapidly, it retains it tenaciously, as shown by the slow disappearance of I^{131} from the thyroid gland. Radioactive iodine liberated by the gland in hormonal form and released in the peripheral tissues is rapidly reaccumulated, making the net change in the gland insignificant. Iodine metabolism in iodine-deficient thyroids must be rapid in order to satisfy the needs of the peripheral tissues; consequently, if the reutilization of inorganic iodine is blocked, the rate at which I^{131} disappears may be expected to increase. Administration of a thyroid-blocking drug to six patients resulted in an increase in the daily renal elimination rate of I^{131} from 0.26% of the dose given to 7.2%; the daily excretion of I^{127} increased by 219 μg. a day. An increase in the liberation rate was also noted when thyrotropic hormone was given intramuscularly to the same six patients while they were still receiving the thyroid-blocking drug; it was accompanied by the sudden appearance of pain, sensitivity, and swelling in the thyroid. Addition of iodine to the diet had little effect on the uptake, which may indicate that the gland was storing up hormones. Administration of desiccated thyroid, on the other hand, was followed in most cases by a decline in the up-take, showing that the sensitivity of the gland to the thyroid administered was normal.

Minerva Medica, Turin

43:645-668 (March 29) 1952

Changes in Blood After Gastric Resection. M. Banche.—p. 645.

Clinical Significance and Diagnostic Value of Skin Reactions to Food Allergens. L. Cerroni.—p. 656.

*Late Results of Ligation of Inferior Vena Cava in Treatment of Cardiac Decompensation. R. Berto and G. Baccaglini.—p. 661.

Ligation of Inferior Vena Cava in Cardiac Decompensation.—Ligation of the inferior vena cava below the point at which the renal veins join it was performed in March, 1950, in a 41-year-old mother of eight children who had cardiac decompensation. From 1945 to 1947 the patient had had frequent fainting spells of one day's duration, with effort dyspnea, difficult breathing at night so that several pillows were needed, edema of the legs, and swelling of the abdomen, especially after meals. Medical therapy did not give good results. The postoperative course was good, and the patient's condition improved. Although she remained in an easy chair most of the time, she was able to breathe more freely and to do light housework. One pillow was sufficient. The pulmonary circulation had also improved. In a follow-up 14 months later the patient was cyanotic, had moderate dyspnea, but had not suffered fainting spells. She had continuous arrhythmia, and an enlarged liver and spleen. Electrocardiograms revealed persisting Wilson's block and signs of subendocardial lesions. The patient died of cardiac decompen-

sation 16½ months after the operation. Autopsy was not permitted. A definitive evaluation of the results of this operation is not possible from this single case. Although the intervention is only palliative in that the patient remains a cardiac patient in need of medical therapy, dyspnea, tachycardia, cyanosis, and edema are decreased, diuresis reactivated, mean pressure increased, and cardiac volume and pulmonary flow decreased. The operation was well tolerated by the patient and proved beneficial, but the anatomicopathological process continued to develop even though the functional lesion seemed to be better tolerated. This operation is contraindicated when there is thrombosis within the heart.

Münchener medizinische Wochenschrift, Munich

94:1057-1104 (May 23) 1952. **Partial Index**

Significance of "Energetic Share of Optic Tract" in Regulation of Metabolism. F. Hollwich.—p. 1057.
Satisfactory Results Obtained with Antistine in Epidemic of Trichinosis; Aplastic Anemia Complicating Trichinosis. H. Mühlbauer.—p. 1065.
Therapy of Thromboembolism in General Practice. W. Greuel.—p. 1069.
*Method for Determination of Gastric Acidity Without Stomach Tube, Based on Radioactive Calcium and Phosphorus Levels in Urine. W. Maurer and A. Zimmer.—p. 1072.

Determination of Gastric Acidity by Radioactive Elements in the Urine.—There are indications that the true gastric acidity may be influenced by the psychical load placed on the patient through the insertion of a stomach tube, the use of which may be contraindicated in certain patients or refused by others. The authors describe a procedure that they consider free of the sources of error and deficiencies associated with the use of a stomach tube. The patients were given 300 mg. of an aqueous suspension of calcium carbonate tagged with radioactive calcium (Ca^{45}). In the stomach, depending on hydrochloric acid secretion, a portion of the tagged calcium carbonate is transformed into radioactive calcium chloride. Only this transformed portion is absorbed by the intestine, while the undissolved portion of the calcium carbonate is excreted in its unabsorbed state. It was assumed that the amount of radioactive calcium (Ca^{45}) in the patients' serum and urine should correspond with the amount of absorbed radioactive calcium chloride. Results showed that definite conclusions concerning the gastric acidity may be drawn from the specific activity of the calcium in the urine. In patients with histamine-refractory anacidity the calcium in the urine was almost inactive. Patients with normal gastric acidity showed considerably higher values, which could be well differentiated from those in patients with abnormal acidity. The same observation had been made previously concerning the activity of the calcium in the patient's serum. The same results were also obtained in patients who were given an aqueous suspension of magnesium pyrophosphate tagged with radioactive phosphorus (P^{32}) instead of calcium carbonate tagged with radioactive calcium. The occurrence of anacidity not refractory to histamine following the insertion of a stomach tube in emotionally labile patients could be prevented completely by the radioactive calcium method. The latter procedure facilitates the control of doubtful results of titration. The tagging doses consisted of several tenths of a microcurie, and were therefore far below the tolerance dose.

Presse Médicale, Paris

60:709-740 (May 14) 1952. **Partial Index**

Study on Microcythemias; Reproduction of Erythrocytes by Budding—Value in General Pathology. P. Brocq and T. Stéphanopoli.—p. 709.
*Cerebral Angiography as Aid in Diagnosis and Localization of Intracranial Hematomas in the Subtentorial Floor: Therapeutic Inferences. D. Petit-Dutaillis, B. Pertuiset and J. Rougerie.—p. 712.
*Cytological Diagnosis of Cancer of Stomach. A. Sicard, E. Périer, R. Godet and V. Besimensky.—p. 720.

Cerebral Angiography in Intracranial, Subtentorial Hematomas.—Unilateral or bilateral carotid arteriographic studies were made percutaneously with a 45% solution of 3,5 diiodo-4-pyridone-N-acetate of diethanolamine on 28 patients with intracranial, subtentorial hematomas. As a routine measure one anteroposterior and three lateral studies were made. Of the 28 patients, 15 had subdural hematomas of the convexity, 1 had a subdural, basilar hematoma, 3 had extradural hematomas, and 9 had intracerebral hematomas. Results showed that arteriography is of diagnostic value for intracranial hematomas following cranial trauma as well as for chronic subdural and nontraumatic intracerebral hematomas. Whereas in such conditions ventriculography may be associated with certain risks, arteriography is well tolerated. The peculiarities in the displacement of the arteries in the authors' cases as opposed to the displacement observed in cases of tumors were an aid in the diagnosis of the lesion and its localization. Although arteriography may somewhat delay surgical intervention, the latter will be facilitated and shortened.

Cytological Diagnosis of Cancer of the Stomach.—Gastric cytological studies of 18 patients with various gastric disorders were made according to the technique of Panico and Papanicolaou. The gastric tissue was obtained with an inflatable abrasive balloon. One patient who was suspected of having cancer and in whom the results of the cytological study were doubtful did not submit to surgical intervention. Nine of the 17 subjected to operation had benign ulcers and one had gastritis, and in all of them the results of the cytological study had been negative. Of the six patients in whom the suspected cancer of the stomach was proved by the surgical intervention, the results of the cytological studies had been positive in four, doubtful in one, and negative in one. In one patient in whom diagnosis of cancer of the stomach had been based on functional signs and impaired general condition, results of the cytological examination were negative, and cancer of the jejunum was revealed by surgical intervention. It seems therefore that results of cytological studies may be correct oftener in patients with benign lesions than in those with malignant lesions. While positive results are of great diagnostic value, one cannot depend with certainty on negative results. The technique used is simple and inoffensive, but occasionally inadequate. Cytolyzed cells may be observed frequently, making interpretation of the smears difficult. Although the cytological method proved less reliable in diagnosing gastric disease than in gynecological conditions, combined with roentgenologic and endoscopic examination it may be of aid in early diagnosis of cancer of the stomach.

Revista Clínica Española, Madrid

44:293-368 (March 15) 1952. **Partial Index**

Brain in Normal and Pathological Old Age. J. Solé Sagarra.—p. 293.
*Arterial Origin of Hypertensive Substance. P. de la Barreda, A. F. Molina, R. Alcalá and C. Jiménez Díaz.—p. 300.
Endocrine Cystic Mastitis and Breast Cancer. E. Roda Pérez and M. Fernández-Criado Pérez.—p. 303.
Topographical Value of Cerebellar Clinical Signs. J. V. Anastasio.—p. 307.

Arterial Origin of the Hypertensive Substance.—The authors believe that the hypertensive substance is a genuine internal secretion from the arterial wall, caused by a sympathetic stimulus acting on the wall. Other workers believe that vagal excitation causes the hypertensive substance to be secreted in the brain acting as a gland of internal secretion. The hypothesis of an internal cerebral secretion is disproved by the results obtained in a new series of experiments: 1. Vagal stimulation of the head of a dog whose circulatory system has been separated into two independent parts, the upper maintained by the heart and the lower by continuous perfusion from a donor dog, produces hypertension not only in the cephalic portion in which the blood passes through the head but also in the lower portion in which the blood does not pass through the head. 2. Similar vagal stimulation no longer produces hypertension in a dog from which a segment of the cervical spinal cord has been removed, even though the blood continues to circulate normally through the head. 3. Similar vagal stimulation when the circulation is interrupted at the neck produces hypertension only so long as the nerve connections between the perfused head and the rest of the body remain intact, and the hypertension so produced occurs not only in the donor dog but also in the lower part of the recipient dog, which does not receive any of the blood that has passed through the head. When the spinal cord is severed and the sympathetic chains are interrupted, the head ceases to transfer hypertensive substances to the donor dog. The hypertensive

substance must therefore originate in the arterial wall; it cannot be a cerebral secretion. The nature of the hypertensive substance is not yet known, but dibenamine® (N,N-dibenyl-β-chloroethylamine) appears to have an inhibitive effect on it.

Revista de Obstetricia y Ginecología, Caracas

12:1-140 (No. 1) 1952. **Partial Index**

Normal Puerperium. C. Nouel.—p. 30.
*Vaginal Trichomoniasis in Pregnant Women. O. Aguero, H. Wallis and A. Marcano.—p. 47.
*Fetal Erythroblastosis. Treatment by Exchange Blood Transfusion. M. Layrisse, A. Sucre, O. Aguero and H. Wallis.—p. 56.

Vaginal Trichomoniasis.—In a maternity hospital of Caracas, the vaginal secretion of 604 women during their first pregnancy was routinely examined for Trichomonas vaginalis. The women were divided in two groups of 244 and 360, respectively, as the secretion was taken from either or both the introitus and the vaginal cul-de-sac. Positive results for T. vaginalis were obtained in 87 women (32%) in the former group and in 108 women (30%) in the latter group. Leukorrhea alone or with pruritus was observed in 78 women (40%) with T. vaginalis and in 102 women (25%) who did not have the parasitic infestation.

Fetal Erythroblastosis.—A case of fetal erythroblastosis successfully treated by exchange transfusion is reported. The mother had previously delivered two normal and six icteric infants. Four of the icteric infants died within three days of birth and two had recovered after repeated blood transfusion. Near full term of her ninth pregnancy her blood showed a high titer of anti-D agglutinins and bilirubinemia. The infant was delivered by cesarean section. He was icteric and had hepatosplenomegaly. A total of 500 cc. was exchanged in increments of 10 cc. from the infant and 10 cc. from a donor. After exchange transfusion the blood became normal, except for moderate anemia that spontaneously disappeared within six months. Exchange transfusion is more valuable than repeated blood transfusion because erythrocytes are supplied to the blood at the same time that hemolyzing maternal antibodies and the products of the breakdown of hemoglobin are removed from it.

Semaine des Hôpitaux de Paris

28:1527-1572 (May 18) 1952. **Partial Index**

Homografts from Bone Bank. J. Hussenstein.—p. 1527.
*Results of Vascular Grafts: Experimental and Clinical Study of Homografts and Heterografts. N. Oeconomos and J. Hewitt.—p. 1538.
Neurological Sequelae After Cardiac Arrest of 15 Minutes. E. Forster, S. Forster and A. Maier.—p. 1547.
Radiological and Radiomanometric Study of the Genital Passages of Man Applied to Clinical Practice and Physiology. J. Boreau, P. Hermann, B. Vasselle and R. Fua.—p. 1549.
General Anesthesia and Bloodless Surgery in Operations for Maxillary Tumors. J. Labayle and F. Roth.—p. 1556.

Homologous and Heterogenous Vascular Grafts.—Vascular grafts may be preserved in physiological liquids, which preserve the vascular fragments in a state of retarded life, or in fixative solutions. The behavior and condition of vascular grafts preserved by various methods has been studied in 50 dogs, some of which were followed for more than a year. Results were judged on the basis of pulse measurements, arteriography, and histological examination of the graft after the death of the animal. Grafts that had been preserved in Gross' liquid for 13 days in one case and four months in another functioned perfectly for more than 18 and 14 months respectively. The host animals remained in good condition, as shown by normal pulse rates and arteriograms. The macroscopic appearance of the grafts was satisfactory, but histological examination revealed significant changes, including calcification. Such changes might gradually transform the graft into a rigid conduit; this would not be serious in short grafts of from 2 to 3 cm. but in long ones of from 8 to 10 cm. or more it might be. Grafts preserved in fixative solutions (4% "formol" [formaldehyde and wood alcohol in water] and 20% alcohol) become calcified and rigid; they serve perfectly as replacement tubes, but their ultimate effect on the vasomotor activity of the recipient artery may prove injurious. Heterografts taken from other animals (calves, sheep, pigs, and horses in particular) remained permeable and satisfactory for the first two to four months, but finally became thrombosed. Establishment of a human artery bank has made grafting operations possible for 18 patients with such conditions as stenosis of the aortic arch, the tetralogy of Fallot, and arterial aneurysms. There have been no deaths attributable to the grafts. In two patients who died from other causes the grafts were found to be satisfactory at autopsy. All the problems connected with the use of preserved arterial grafts have not yet been solved, however, and they should not be used except in cases of absolute necessity.

Strahlentherapie, Munich

87:1-160 (No. 1) 1952. **Partial Index**

Pathological Aspects of Carcinoma of Breast. W. Ceelen.—p. 7.
Irradiation Therapy of Cancer of Breast. H. Meyer.—p. 35.
Early Results of Preoperative Irradiation of Breast Cancer. W. Oelssner.—p. 49.
Combined Therapy of Metastasizing Mammary Carcinoma. F. Handel and K. Meinardus.—p. 53.
*Mammary Carcinoma and Pregnancy. F. Remold.—p. 65.

Carcinoma of Breast and Pregnancy.—The association of breast carcinoma and pregnancy is comparatively rare. At the women's clinic at the University of Erlangen only 36 such cases were observed among a total of 2,455 cases of carcinoma of the breast (1.46%). Analysis of this material convinced the authors that the prospects of cure are decidedly reduced if pregnancy is associated with carcinoma of the breast, but treatment of the carcinoma must not be postponed. The harmful effect of the pregnancy on the breast carcinoma is especially pronounced during the early stage of pregnancy and during lactation. If pregnancy occurs in a woman who has been treated for mammary carcinoma, relapse and metastasis to the formerly uninvolved breast occur frequently. When the pregnancy was interrupted while the carcinoma was treated, the effect was always unfavorable, because abortion influences the hormone exchange in a way similar to delivery at term, even if the pregnancy has existed for only eight weeks. Since pregnancy even after several years of freedom from recurrence is not without danger, a castration dose of roentgen irradiation is not only of therapeutic but also of prophylactic value.

Zentralblatt für Chirurgie, Leipzig

77:609-640 (No. 15) 1952. **Partial Index**

*Chylothorax; Surgical Anatomy and Roentgenological Demonstration of Thoracic Duct. K. Zuschneid.—p. 609.
Chylothorax; Symptomatology and Etiology. O. Hueck and H. Kahle.—p. 618.
Total Extirpation of Stomach. G. Barthold.—p. 622.
Strangulated Hernia. E. Seifert.—p. 625.

Chylothorax.—Anatomic and physiological studies reported by American and German workers, as well as the satisfactory results obtained by the author with surgical intervention on the thoracic duct in two cases of chylothorax, demonstrated that Florer and Ochsner's statement that direct surgery to repair the thoracic duct results in 100% operative mortality is no longer valid. A new approach to this problem is required because of the increased incidence of unintentional injuries to the thoracic duct, which may be expected during intrathoracic surgical interventions such as Peet's splanchnicectomy. Ligature of the injured thoracic duct is the logical method from the physiological point of view, because flow of lymph is insured by the formation of a collateral circulation. Integrity of the thoracic duct is not indispensable for life to continue. The high mortality rate of an inadvertent operative injury to the thoracic duct or of rupture of the thoracic tract due to an accident makes it necessary to limit conservative procedures in chronic-recurrent chylothorax; thoracotomy and ligature of the thoracic duct is indicated. The surgical approach by transpleural route is relatively simple and prevents recurrent chylothorax. The thoracic duct may be visualized on roentgenograms easily with 20 cc. of a 20% solution of methylglucamine salt of 3,5-diiodo-4-pyridon-N-acetic acid ("perabrodil") in the course of the surgical intervention, and occasionally it may be of significance for differential diagnosis in cases of chylothorax of doubtful origin. In addition, roentgenologic demonstration of the thoracic duct by contrast medium shows the relation of the duct to other organs in the supraclavicular region better than any other method.

BOOK REVIEWS

Vascular Diseases in Clinical Practice. By Irving Sherwood Wright, M.D., Professor of Clinical Medicine, Cornell University Medical College, New York. Second edition. Cloth. $8.50. Pp. 552, with 116 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1952.

A generally increased interest in peripheral vascular diseases makes this useful clinical manual a welcome addition to the literature. In 1948, the first edition of the book was published, and it attained the popularity and wide use that it merited. During the intervening years additions to the medical literature have been reviewed by the author and pertinent new material added. Much of the older text has been revised and brought up-to-date.

The book is essentially a clinical manual for ready reference for those in general practice, internal medicine, surgery, or medical school. The first chapter, devoted to the classification of peripheral vascular diseases, follows the nomenclature of the American Heart Association. In the section on methods of examination, there is a complete review of all the important tests and procedures. Each test is precisely described, and normal and abnormal findings are discussed. A close study of the material in this chapter will give the practitioner and student a basic understanding of peripheral vascular diseases.

The remainder of the book is devoted to discussion of both the important and the less commonly seen diseases. Each chapter follows the traditional pattern of discussion, with material on etiology, pathology, signs and symptoms, diagnosis, and treatment. The sections on pathology are considered from a dynamic viewpoint that includes pathogenesis and progressive change as the disease develops. The subsections on management are clearly presented and reflect the broad experience and mature judgment of the author. Many of the experimental and clinical studies of the author and his associates are neatly summarized in the manual. Certain chapters are exceptionally good; for example, the chapter on neurovascular syndromes of the shoulder girdle reflects much of the author's original work in that field, and the chapter on syndromes produced by temperature changes gives clear descriptions of many disorders that are frequently poorly understood by the average physician. It is gratifying that Raynaud's syndrome, not always comprehended by practitioners, is adequately reviewed and related conditions discussed. The inclusion of chapters on disturbances of the lymph vessels adds much to the value of the book. Physicians in industrial practice will find the chapter on medicolegal problems useful.

The book is written in an interesting, informative, and concise style that will be helpful to both physicians and students. Black and white photographs, color plates and line drawings, and graphs, charts, and tables illustrate important clinical and pathological points. There is a good index. Although the scope of the book is great, the author has reduced the size so that it will be a useful guide to all those interested in peripheral vascular diseases as encountered in clinical practice.

Text-Book of Ophthalmology. Vol. V: The Ocular Adnexa. By Sir Stewart Duke-Elder, K.C.V.O., M.A., LL.D., Surgeon Oculist to H. M. The King. Cloth. $22.50. Pp. 4631-5713, with 1181 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1952.

When the first volume of Duke-Elder's monumental work appeared, one reviewer aptly commented, "This first volume is in our judgment a great book. It is great by reason of its bulk, for it exceeds a thousand pages: it is great in its conception, and also great in its achievement." As the next three volumes came forth, other book reviewers wrote in a similar vein. One said, "For the ground it covers, this book has practically the value of a whole library." A second reviewer stated, "It goes without saying that a book of this kind should be the indispensable possession of the ophthalmologist who values a knowledge of his subject, and more particularly of one whose duty it is to instruct students." A third reviewer wrote, "Anglo-Saxon ophthalmology owes a real debt of gratitude to Duke-Elder, not only for his brilliant research work but even more for his textbook."

That these quotations are by no means exaggerated estimations is quickly made evident by perusal of volume 5, which confines itself to a discussion of the ocular adnexa in five gigantic chapters that deal exhaustively and brilliantly with developmental anomalies, diseases of the lids, diseases of the lacrimal apparatus, diseases of the orbit, and diseases of the para-orbital regions. Some years ago, a reviewer for THE JOURNAL wondered whether the author could possibly maintain such high standards in each succeeding volume. There is no question that Duke-Elder not only has not lost his magic touch but that, with this latest volume, he has welded another scintillating link in a chain of ingenious accomplishment.

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association with the Comments That Have Appeared in the Journal of the American Medical Association, 1951. Cloth. $2. Pp. 165, with illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1951.

A number of the reports included in this volume represent continuations of the work of subcommittees of the Council. The most voluminous of these concerns the use of steroid hormones in the treatment of advanced mammary cancer. The report definitely outlines the status of this therapy but states that "the best curative measure for mammary carcinoma available at present is early diagnosis and radical removal of the tumor and secondary tissue." Related to this is the status report on the much discussed "krebiozen," which analyzes the case histories of 100 patients and finds evidence of "temporary improvement" in only 2. The report definitely brands "krebiozen" as a "secret remedy" and thus may be considered the only "condemnatory" report in this volume.

The two careful and informative studies on benzene hexachloride and chlorophenothane (DDT) represent a continuation of the work of the Council's Committee on Pesticides, a brief statement on the necessity for more accurate and factual death certificates being added as a plea for help in the effort to reduce the loss of lives from careless use of highly toxic products.

The two reports by Dr. Henry K. Beecher and associates, "Narcotics in Preanesthetic Medication" and "A Controlled Study of Pain Relief by Intravenous Procaine" admirably represent controlled studies in the field of pain relief. The former concludes that in preanesthetic medication this function can be "adequately fulfilled by a small dose (90 mg.) of pentobarbital sodium" without recourse to the commonly used narcotics. The second study concludes that "The degree of relief produced by procaine approximates that produced by 90 mg. of pentobarbital sodium" but points out the occurrence of "frequent unpleasant and sometimes serious side reactions" and advises that intravenous procaine has no place in the treatment of pain "unless it can be demonstrated to produce significant beneficial effects on specific disease-processes."

The 11 remaining reports in this volume are all timely and authoritative. Among those worthy of special mention are: "Fluoridation of Water Supplies," which is favored; "Status of Blood Substitutes," which encourages further studies of synthetic preparations but advises restriction to investigational use until more is known of their effectiveness and ultimate metabolism; "Radioisotopes," which outlines the present status of these agents in medical research, diagnosis, and therapy; and "Chemotherapy of Tuberculosis in Man," a report from the Veterans Administration, which concludes that none of the newer antibiotics or other agents compares favorably with the streptomycins. The volume is adequately indexed.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Geschwülste des Ohres und des Kleinhirnbrückenwinkels. Von Dr. med. K. Graf, Priv.-Doz. für Ohren-Nasen-Halsheilkunde an der Universität Zürich. Cloth. 43 marks. Pp. 283, with 132 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

The author has had the opportunity to assemble the studies of 40 cases from the Professor Nager's Clinic. He rightfully feels that a knowledge of tumors of the cerebellopontine angle should be of interest to the otologist (this being Graf's field), the neurologist, the neurosurgeon, and the nonspecialist. In a well-organized monograph, he develops the historical background of acoustic tumors with an inclusion of the rich literature that has accumulated since 1777 when Sandifort described the first case. A bibliography of over 1,000 references attests to the completeness of the exposition. The story unfolds itself in the classical manner, in the analysis of the histories of acoustic tumor patients, their symptoms and diagnostic features, involved neighboring neural parts, roentgenographic features, and spinal fluid findings. The author devotes 16 well-illustrated pages to the roentgenogram changes observed in the internal auditory canal and records the results of a personal study of the width and length of the porus and internal meatus. He develops the thesis of Verocay that the tumor is a neurofibroma or a fibroneuroma that is not malignant and does not produce metastases. Based on a study of 16 histological temporal bone series, Graf does not believe the increased pressure produces a hydrops of the labyrinth. He found the nerve fibers and the ganglion atrophic, but the organ of Corti was well preserved, although there was no response to the caloric and hearing tests. He suggests the removal of the tumor by the neurosurgeon and contends that since tumor masses remain in the internal auditory canal, a second session is indicated by an otosurgical approach. Neuromas of the trigeminal, facial, glossopharyngeal, and vagus nerves, meningiomas, angiomas (glomus jugulare and tympanicum), carcinoma and sarcoma, metastatic forms (hypernephromal), and cholesteatoma are discussed in an interesting manner, supported by case reports. Arachnoiditis is also briefly discussed. This is a valuable addition to the clinical and histopathological study of acoustic tumors and those neoplasms in the posterior fossa that are related to the petrous bone. The meticulous study of the author's cases and the review of the literature should make this monograph a valuable addition to any otological and neurological library.

The Phosphatides. By Harold Wittcoff, Research Dept., General Mills, Inc., Minneapolis. American Chemical Society monograph series. Cloth. $10. Pp. 564. Reinhold Publishing Corporation, 330 W. 42nd St., New York 18, 1951.

The publishers of this monograph state that this is the first complete work on phosphatides in over 20 years. During this period much information has been made available on their chemical structure, purification, analysis, occurrence in nature, biochemical and physiological roles, and industrial applications. The author deals with each of these aspects in turn. He covers the literature through 1949 thoroughly and incorporates the most important 1950 developments. A valuable feature of the work is his discussion of lipid nomenclature in various parts of the world and his careful usage of one system, that adopted by the American Chemical Society. The bibliographies and indexes are good. The printing and binding are up to the high standard of American Chemical Society monographs.

Medical Disorders of the Locomotor System Including the Rheumatic Diseases. By Ernest Fletcher, M.A., M.D., M.R.C.P., Physician-in-Charge of Department of Rheumatism and Lecturer on Rheumatic Diseases, Royal Free Hospital, London. Second edition. Cloth. $11. Pp. 884, with 376 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1951.

This comprehensive volume is an excellent reference book for anyone interested in disorders of the locomotor system and rheumatic diseases. It should be of particular value to the internist, the neurologist, the orthopedic surgeon, and the general practitioner. It is too detailed and too long to be used as a textbook for students, although even for them it is a good reference book.

The author has planned the book well, and the various chapters are subdivided, allowing one to read a particular section of the book and obtain the greatest amount of information from each chapter. The chapter on physical examination should be carefully read, for the author emphasizes the fact that the examination of the patient should be done more carefully in order to evaluate the symptoms. The chapters on anatomy and the anatomy and physiology of bone are excellently written. The sections devoted to rheumatic fever and arthritis are also well written. The latter part of the book, which discusses orthopedics, deals with the peripheral neuritides, muscle nerve testing, peripheral vascular disorders, foot strains, and allied conditions.

The authors are to be commended on the general excellence of the book. Their combined experience, published in one volume, is indeed an excellent contribution to 1952 literature.

God and Man at Yale: The Superstitions of "Academic Freedom." By William F. Buckley, Jr. Introduction by John Chamberlain. Cloth. $3.50. Pp. 240. Henry Regnery Company, 20 W. Jackson Blvd., Chicago 4, 1951.

This extremely well-written book traces the development and dominance of agnosticism and collectivism in the texts and teachings in one of our oldest universities. Yale was founded to upraise spiritual leaders and has been supported by the fruits of a free economy. It is supposedly one of the more conservative institutions of higher learning. According to the author, its students are exposed to predominantly antireligious and frankly collectivist doctrines in the courses that deal with economics and religion, outside of the School of Religion. The evidence presented indicates that religion is neglected or derided in most of these courses but is convincing in the field of economic theory and practice. The author supports his case by extensive quotations from texts and from lectures and statements by professors.

The book is well worth reading for anyone interested in education and its influence on the course of American life. One disturbing feature is that if these conditions exist at Yale they must be widespread in other educational institutions and are probably far more aggravated in some. He carefully differentiates between true academic and scientific freedom and the abuse of the term "academic freedom," which is used as a basis for teaching doctrines that are contrary to what he and many others consider the fundamental concepts of American freedom. These concepts have stood the test of time, have provided more good for more persons, and have established a higher level of ethical conduct than have the ideologies advocated by some texts used at Yale and taught by certain professors. The author suggests what appear to be reasonable methods of correction of the conditions to which he objects. These would apply with varying influence to other institutions and should be of great interest to the alumni bodies of all universities.

Elementary Medical Statistics: The Principles of Quantitative Medicine. By Donald Mainland, M.B., Ch.B., D.Sc., Professor of Medical Statistics, Division of Medical Statistics, Department of Preventive Medicine, New York University College of Medicine, New York. American monograph series [4]. Boards. $5. Pp. 327, with 2 graphs in separate pocket. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1952.

A considerable number of books on elementary medical statistics are now available, some useful only in special situations, others written with sufficient discernment and imagination to be generally adaptable to the needs of American medical students. Mainland's book belongs to the latter category and should prove helpful in the hands of a capable teacher. As the author intimates in his preface, one should not be too enthusiastic about seeing statistics established as a subject in the undergraduate curriculum, for in the hands of some instructors the emphasis on memorizing, on techniques, and on preparation for board examinations is a handicap. To combat the perennial tendency toward static pedagogy there is need of recognition of the importance of the subject by the administrative officers and a constant effort by a sincere and versatile instructor. The present book supplies a wealth of material about which a good introductory course can be organized. Because of the elementary nature of the book, certain topics will be missed by some readers; in particular, one might wish for some discussion of mortality tables. In general, however, the book has the advantage of illustrating principles by well-chosen medical instances, and it can be recommended as both accurate and attractive.

QUERIES AND MINOR NOTES

BIRTHS IN HOSPITALS

TO THE EDITOR:—*The statement has been made that pain relief in labor is used extensively in the United States, where more than 90% of births occur in hospitals. I cannot believe that 90% of all deliveries in the United States occur in hospitals, and, incidentally, I would consider it a sad commentary if this were so. I would appreciate a breakdown of the population figures for the United States into urban and rural populations and the percentage of total births that occur in the hospital in each group.*

N. W. Haas, M.D., San Benito, Texas.

ANSWER.—A report of the National Office of Vital Statistics (vol. 36 [July 2] 1951) illustrates clearly the tremendous increase that has occurred in the utilization of hospital facilities for maternity care. This bulletin shows that the annual number of live births in the United States increased from 2,155,105 in 1935 to 3,559,529 in 1949, while in the same period the percentage of hospital births advanced from 36.9% to 86.7%. In some areas, as shown in the accompanying regional classification for 1949, the hospital births were well in excess of 90%. The rates, it will be noted, are generally higher in the urban centers, which range from 81.1% to 98.9% as compared with 48.5% to 97.5% in rural sections.

Area	Est. Population (Bureau of Census)	No. of Live Births	Hospital Births, %		
			Total	Urban	Rural
New England	9,364,000	196,170	97.7	98.9	94.3
Middle Atlantic	29,944,000	623,474	96.0	97.8	90.8
East North Central	30,114,000	713,082	94.9	96.6	91.3
West North Central	13,723,000	330,487	93.1	97.0	88.8
South Atlantic	20,719,000	537,814	70.7	87.0	58.8
East South Central	11,210,000	309,884	59.8	81.1	48.5
West South Central	14,266,000	373,095	77.4	85.8	67.2
Mountain	4,854,000	138,406	91.3	95.1	87.0
Pacific	14,365,000	337,057	98.3	98.8	97.5
Total	148,558,000	3,559,529	86.7	94.3	75.8

MYASTHENIA GRAVIS AND PREGNANCY

TO THE EDITOR:—*A 26-year-old married woman is pregnant, Nov. 18, 1952, being the expected date of confinement. Three and a half years ago, a diagnosis of myasthenia gravis was made, and since then the patient has been taking a maintenance dose of 4 to 15 tablets (15 mg. each) of neostigmine (prostigmine®) bromide daily, varying the dosage according to her own subjective symptoms. Because of previous miscarriages, at three and five months seven years ago, she has been taking diethylstilbestrol (5 mg. four times a day) and thyroid (0.03 gm. daily). In regard to the myasthenia, what complications may be expected during the last trimester of pregnancy, the labor, delivery, and immediate postpartum period? Does the use of neostigmine bromide, which is mandatory, contraindicate the use of other drugs?*

N. Z. Grover, M.D., North Hollywood, Calif.

ANSWER.—As far as is known, there are no special complications to be expected during pregnancy or labor in a patient with myasthenia gravis, except in cases of the so-called bulbar type, which is much more serious. Therapy, of course, should be continued and should be adequate, as mentioned. There are no contraindications to using drugs usually used in pregnancy and labor. Anesthesia should be minimal, and the patient should be watched carefully until fully recovered from the anesthesia.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

SOUND WAVES AND KIDNEY STONES

TO THE EDITOR:—*A patient has had recurrent kidney stones, and now has one that seems to be too large to pass through the ureter. Is it possible to break up kidney stones or stones in the ureter with sound waves so that they can pass through the ureter? Is there any other method available to accomplish this in order to avoid surgical intervention?* *M.D., New York.*

ANSWER.—There is no method available by which a kidney or ureteral stone can be fragmented or dissolved by sound waves. Some fundamental research has been carried out with this in mind, but as yet there has been no practical application of this method.

SCLERODERMA

TO THE EDITOR:—*A woman, aged 40, with scleroderma, has a basal metabolic rate of +9%, and she is slightly anemic. Because of the positive metabolic rate I cannot give her large doses of thyroid. Another physician has been treating her with corticotropin (ACTH) and cortisone, with no improvement. What would be the best treatment, aside from a hematinic, small doses of thyroid, and estrogenic hormones?*

Carrie Anderson-Robinson, M.D., Boulder, Colo.

ANSWER.—The treatment of scleroderma is extremely unsatisfactory. The disease usually progresses in spite of treatment. The rate of progress will vary in the individual case. At the present time an endocrine factor seems a major one. Thyroid in small doses is advisable. Estrogens are used frequently. Becker speaks of two patients who were helped with raw pancreas. Vitamin A has been used in fairly large doses. Symptomatic treatment is important in the long range treatment of the patient. Hot soaks, sunlight, massage, baking, a warm climate, and treatment of the anemia can give valuable assistance.

TRICHOMONAS URETHRITIS IN THE MALE

TO THE EDITOR:—*For the past six months a 19-year-old youth has had urethritis and prostatitis caused by Trichomonas. Treatment has included all the antibiotics, sulfonamides, massage, intraurethral instillations of aureomycin ointment, and acidification of the urine. Though there have been sporadic improvements, urethroscopy still reveals an infected posterior urethra. Is there anything further to try?*

Gottlieb Helpern, M.D., New York.

ANSWER.—Prostatic massage at regular intervals should be continued. Daily anterior-posterior intraurethral instillations of acriflavine in a dilution of 1:4,000 would be helpful. Carbarsone, 0.25 gm. four times daily, may aid in the eradication of the trichomonads from the prostate. It is assumed that the patient is not being reinfected by marital or extramarital exposure. Stricture is also an etiological factor in the persistence of these infections, but here this would not seem likely since urethroscopy has been done.

HYPOTHYROIDISM AND TUBERCULOSIS

TO THE EDITOR:—*Is there any contraindication to using thyroid pills, 1 or 2 grains (0.06 or 0.13 gm.), daily in a woman, aged 40, who has a basal metabolic rate of −35% and a minimal apical active tuberculous lesion that has been undergoing slow fibrosis for one year?* *M.D., Minnesota.*

ANSWER.—There is a prevailing impression that an excess of thyroid secretion is protection against tuberculosis and also that tuberculosis and hyperthyroidism rarely occur together. In fact, it is felt that hypothyroidism may predispose to tuberculosis. Some reports of the heightening of tuberculin sensitivity in patients with hypothyroidism after administration of thyroid substance have appeared in the literature. From this it would seem that it would be quite proper to administer thyroid as indicated to a patient with combined pulmonary tuberculosis and hypothyroidism.

PHENOBARBITAL

To the Editor:—*Is it harmful to give patients aged 60 or over phenobarbital, ¼ grain (0.05 gm.) three times daily, for the treatment of such conditions as hypertension, coronary artery disease, and spastic colitis? Does it accumulate in the body and become toxic, causing permanent damage to the central nervous system, liver, kidneys, blood forming organs, and other tissues?* *M.D., Tennessee.*

Answer.—There would be very little danger in the administration of such small amounts of phenobarbital to patients of the type mentioned. With such doses of phenobarbital, cumulation would not be likely to occur, and no permanent damage to any organ would be anticipated. Occasionally sensitivity develops to any of the barbiturates and is most often manifested by a skin eruption. This occurs so rarely that phenobarbital is regarded as one of the safest drugs for long-continued, mild sedation.

RADAR AND CATARACTS

To the Editor:—*A patient, aged 20, with no family history of cataracts, has rapidly progressing cataracts in both eyes. The left eye in which vision has decreased from 20/30 to 20/70 in a few months, has a severe rosette shaped, feathery cataract. It is subcapsular anterior and posterior, with diffusely scattered dots through the lens. The right eye has early changes of the same type. The patient works close to radar as a repairman.* *M.D., Washington.*

Answer.—Radar waves are completely absorbed by the cornea and have not been reported to be a cause of cataract. The Grotthus-Draper law requires that absorption of radiation must take place for a reaction to be produced. Thus, in the absence of penetration of the cornea, radar waves will not cause any change in lens transparency.

ROENTGENOGRAPHIC EXAMINATION OF TEETH

To the Editor:—*What is the consensus regarding roentgenographic examination of the entire mouth every 6 months, beginning at the age of 6 years, for detecting dental cavities?* *M.D., Pennsylvania.*

Answer.—Dental authorities agree that roentgenographic examination of all the teeth is necessary for making a thorough dental diagnosis; however, it is not possible to establish hard and fast rules as to the need for making a complete roentgenographic examination every six months for every patient. It is considered good practice, on the other hand, to use bite wing x-ray films for each examination as an aid in detecting carious lesions as early as possible.

DIARRHEA FOLLOWING ILEECTOMY

To the Editor:—*A 38-year-old woman had eight operations for adhesions and bowel obstruction following pelvic inflammatory disease. At the last operation, 5 ft. of hopelessly involved terminal ileum was removed, leaving the gastrointestinal tract in comparatively excellent condition. Now she has about eight stools a day, this in spite of diet and medication. What treatment do you suggest?* *A. A. Skemp, M.D., LaCrosse, Wis.*

Answer.—Diarrhea following resection of a considerable segment of the small bowel is not an unusual complication and in the vast majority of cases remedies itself with the usual type of treatment. There appear to be no specific remedial agents for this complication.

ARTHRITIS IN DIABETICS

To the Editor:—*Please advise present day treatment and management of rheumatoid arthritis in diabetics receiving insulin, when therapy is instituted in the office.* *M.D., New York.*

Answer.—The treatment of rheumatoid arthritis in diabetics is the same as that in nondiabetics, with the exception that if a diabetic patient is given cortisone or corticotropin, it must be borne in mind that these drugs may temporarily increase the blood sugar level and the insulin requirement.

ALKALINE URINE

To the Editor:—*How can the urine of a patient on a low sodium diet be rendered alkaline?* *M.D., Ohio.*

Answer.—Patients on a low protein diet, with a liberal allowance of fruit and fruit juices, usually have a neutral or alkaline urine, as do all the herbivorous animals. If their caloric needs are not met by fat and carbohydrate, the urine may become acid, as in fasting herbivorous animals. Adding sodium chloride to either diet has little effect on urinary acidity. If a patient on a vegetable diet low in sodium has an acid urine, it would be possible to give citrus juices or potassium citrate to cause it to become alkaline. In severe renal failure, with diminished capacity for renal ammonium synthesis, there is risk of hyperpotassemia if such a diet is employed.

THICKENED TOENAIL

To the Editor:—*Please suggest how to overcome the ingrowing tendency of a thickened nail that is regrowing after a crushing injury of the distal phalanx of the great toe?* *M.D., California.*

Answer.—The thickened nail should be trimmed from time to time with a strong-jawed nail clipper. The dead skin underneath the removed nail should also be thoroughly cleansed away. These nails often become chronically infected by a fungus. In such cases an antimycotic dye, such as malachite green or gentian violet, is useful, and sometimes x-ray treatment is beneficial. In troublesome and persistent cases, it may be advisable to remove the entire nail bed so that the nail cannot reform.

MÉNIÈRE'S SYNDROME

To the Editor:—*Has procaine hydrochloride any value in the treatment of Ménière's syndrome? If so, what dosage and route of administration are advised? A patient noticed cessation of the ringing in her right ear during anesthetization of the homolateral jaw by procaine hydrochloride in a dental procedure.* *M.D., Wisconsin.*

Answer.—There is no reliable evidence to indicate that procaine hydrochloride as employed is of value in the treatment of Menière's syndrome.

PENICILLIN IN MEASLES

To the Editor:—*In cases of measles does the administration of penicillin to quell the fever delay the eruption?* *Walter A. Landry, M.D., Chester, Pa.*

Answer.—Penicillin administration seems to exert no influence on the development or duration of the measles rash. The chief purpose of penicillin for measles is its prophylactic or therapeutic action in respect to bronchopneumonia.

TIN PREPARATIONS IN ACNE

To the Editor:—*Please advise how successful the use of tinpronate® has been in the treatment of acne? Is its use contraindicated for prolonged treatment?* *J. H. Turner, M.D., Huntington Park, Calif.*

Answer.—Tin preparations for the treatment of infections enjoyed a vogue for only a short period and even then were not employed by experienced physicians. They proved altogether worthless for the treatment of acne, for this is a condition with many causative factors. No one drug is effective in all cases.

PHENOBARBITAL IN HEART DISEASE

To the Editor:—*What harmful results, if any, follow the prolonged daily use of phenobarbital sodium in patients with heart disease?* *John H. Robertson, M.D., Binghamton, N. Y.*

Answer.—There has been no evidence of any harmful effect of the daily use of small doses of phenobarbital sodium on the human heart whether there is heart disease present or not.